

The Failure of Compulsory Licensing of Pharmaceuticals in Least Developed Countries

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vorgelegt von

Name: Stephan Brebeck

Geburtsort: Düsseldorf

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Erstgutachter: Herr Professor Dr. Stefan Felder

Zweitgutachten: Herr Professor Dr. Erwin Amann

Short Table of Contents

1. Introduction	1
2. TRIPS Agreement and Flexibilities	14
3. Static Impact of Compulsory Licensing	40
4. Dynamic Aspects: Incentives	65
5. Dynamic Aspects: Negotiations	87
6. Open Economy	107
7. Summary, critique and further research	121
Bibliography	124
A. Appendix	139

Abstract

With its ratification in 1995 the World Trade Organization's agreement on "Trade Related Aspects of Intellectual Property Rights" (TRIPS) advances minimum global patent protection. Particularly in view of access to essential medicines the TRIPS agreement permits countries to overwrite patent exclusivity in isolated cases and compulsory license a domestic manufacturer. Subsequently, export of compulsory licensed drugs was authorized to account for the lack in appropriate drug production capabilities of least developed countries. So far, this cross border compulsory licensing was used only once, in contrast to numerous domestic utilizations. While literature highlights political pressure and threads to foreign direct investment as general barriers for compulsory licensing the question remains why only least developed countries do not make use of this instrument. The work at hand contributes to the debate by identifying a discrimination of least developed countries which roots in the mechanics induced by the compulsory licensing process itself. A private generic manufacturer would not sell a compulsory licensed drug at marginal costs but determine the optimal duopoly competition price for a given structure of demand. Since potential licensees apply for compulsory licensing the optimal price is overwritten by negotiations and usually reduced significantly. This does not hold for least developed countries seeking cross border compulsory licensing because the sequence of price bids and decision is different. As a result, cross border compulsory licensing loses its appeal, further reduced by royalty and transportation cost effects on the generic price.

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Declaration

I, the undersigned, hereby declare that this dissertation entitled, "The Failure of Compulsory Licensing of Pharmaceuticals in Least Developed Countries" is my own work, and that all the sources I have used or quoted have been indicated or acknowledged by means of completed references.

Mainz, 17.09.2013

Place, Date

Stephan Brebeck

List of Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ARV	Antiretroviral
CAMR	Canada Access to Medicines Regime
CBCL	Cross Border Compulsory Licensing
CL	Compulsory Licensing
DCL	Domestic Compulsory Licensing
G	Government
GATT	General Agreement of Trades and Tariffs
GC	Generic Competitor/ Manufacturer/ Licensee
GSK	GlaxoSmithKline
HIV	Human Immunodeficiency Virus
ICL	Import Compulsory Licensing
IPR	Intellectual Property Rights
IV	Innovator
LDC	Least Developed Country
LIE	Low-Income Economies
LMIE	Lower-Middle-Income Economies
MRSCA	Medicines and Related Substances Control Amendment
MSD	Merck Sharp and Dohme
MSF	Médecins Sans Frontières
NGO	Non-Governmental Organization
R&D	Research and Development
TRIPS	Trade-Related Aspects of Intellectual Property Rights
TRM	Tiered Royalty Method
UMIE	Upper-Middle-Income Economies
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

List of Figures

1.1. Definition of Neglected Diseases	8
1.2. Allocations of R&D for neglected diseases	9
1.3. Neglected diseases funding development by tiers	10
1.4. HIV/AIDS R&D funding by funder types	11
1.5. Dengue R&D funding by funder types	12
2.1. Number of issued compulsory licenses by year	33
2.2. Number of compulsory licensing episodes by year	34
2.3. Compulsory licensing episodes by country income groups	35
3.1. South Africa Distribution of Income	46
3.2. Exemplary South Africa demand curve	47
3.3. Exemplary South Africa sales revenue	47
3.4. Exemplary Norway sales revenue	47
3.5. The innovators profit without royalty	54
3.6. Separated effects of royalty on generic price	61
4.1. Patent buy-outs with follower but without joint randomization	78
4.2. Patent buy-outs with follower and joint randomization	79
4.3. Fund allocation of advanced market commitment pilot	83

5.1. Representation of extensive negotiation game N	90
5.2. Compulsory licensing episodes by outcome	94
5.3. Compulsory licensing episodes by disease group	96
5.4. Representation of extensive application game A	97
5.5. Example of game \tilde{A} with outcome no CL	104
5.6. Example of game \tilde{A} with outcome CL	105
6.1. Representation of extensive commitment game C	115
A.1. Complete list of compulsory licensing episodes (additional information)	141

List of Tables

2.1. List of compulsory licensing episodes	32
3.1. Estimated cross-price elasticities by Chaudhuri, Goldberg, and Jia (2003)	43
3.2. Compulsory licenses and remuneration	55
5.1. Compulsory licensing episodes with discount outcomes	95

Detailed Contents

Short Table of Contents	I
Abstract	I
Acknowledgement	II
Declaration	III
List of Abbreviations	IV
List of Figures	IV
List of Tables	VII
Detailed Contents	VIII
1. Introduction	1
1.1. Structure and Literature	2
1.2. Diseases Predominantly Affecting the Poor	7
2. TRIPS Agreement and Flexibilities	14
2.1. From Paris Convention to TRIPs	16
2.2. Compulsory Licensing	19
2.2.1. Compulsory Licensing under Domestic Production	20
2.2.2. Import Compulsory Licenses	24
2.3. Doha Declaration	27
2.4. Utilization Assessment	31

2.5. Debate Outline	36
2.6. Conclusions and Outlook	37
3. Static Impact of Compulsory Licensing	40
3.1. Drug Demand Characteristics in Light of Neglected Diseases	42
3.1.1. The Domestic Competitor's Distribution Network Advantage	42
3.1.2. The Innovator's Quality Advantage	44
3.1.3. Income Inequality and Neglected Diseases	45
3.2. Asymmetric Duopoly Model	48
3.3. Remuneration and Compulsory Licensing	55
3.3.1. General Royalty Effects on the Licensee's Price	56
3.3.2. Exemplary Demonstration of Royalty Effects	59
3.4. Conclusion	61
4. Dynamic Aspects: Incentives	65
4.1. Incentives for Pharmaceutical Research	66
4.1.1. Economics of Patents	67
4.1.2. Patent Critique & Industrial Drug Development	71
4.2. Alternatives	74
4.2.1. Patent Buyout Mechanism	74
4.2.2. The Health Impact Fund	80
4.2.3. Advanced Market Commitments	82
4.3. Conclusion	84
5. Dynamic Aspects: Negotiations	87
5.1. Compulsory Licensing as a Threat	89
5.2. Generic Competitor as an Applicant	96
5.3. Application of Discrete Asymmetric Demand Model	102

5.4. Conclusion	105
6. Open Economy	107
6.1. Free Riding, Differential Pricing and Parallel Imports	108
6.2. Cross Border Compulsory Licensing	111
6.2.1. Royalty and Cross Border Compulsory Licensing	113
6.2.2. Negotiations and Cross Border Compulsory Licensing	115
6.3. Conclusion	119
7. Summary, critique and further research	121
Bibliography	124
A. Appendix	139
A.1. Details on Compulsory Licensing Assessment	139
A.2. Excerpt: Agreement on Trade Related Aspects of Intellectual Property Rights	142
A.3. Implementation of Paragraph 6 of the Doha Declaration on the TRIPs Agreement and Public Health	144

1. Introduction

The work at hand contributes to the economic evaluation of pharmaceutical patent protection in the developing world. It does not attempt to analyze the trade-off between incentives for research and access to medicines. Without taking sides in this serious problem we look at the current situation of global intellectual property rights as mandated by the World Trade Organization (WTO) and at the national implementation. We investigate the induced mechanics and find that the current system discriminates least developed countries unintentionally.

The focus lies on a derogation conceded to developing countries by the WTO in the agreement on "Trade Related Aspects of Intellectual Property Rights" (TRIPS), compulsory licensing (CL). Generally, the TRIPS agreement from 1995 establishes minimum patent protection of 20 years for member countries. The CL derogation allows governments to license generic manufacturers for production and marketing of a patented drug without authorization of the right holder. Advocates of compulsory licensing argue that developing countries need this measure to increase accessibility to drugs in the fight against diseases highly prevalent in the poor population, especially those which are communicable. Compulsory licensing in its form today is the result of negotiations and concessions on the way to global patent protection, but the topic is underrepresented in economic literature. While it is not possible to ultimately assess

the impact of wide compulsory licensing usage by preventing patent protection on access and innovation, this thesis draws conclusions based on the mechanics induced.

The analysis points out that compulsory licensing is most likely to be issued for drugs addressing neglected diseases and thus jeopardizes any positive effect on innovation regarding these diseases that global patent protection could have had. This leads to a situation in which developing countries accept patent protection for drugs on which they could free-ride on innovation while undermining it for diseases that only they can set incentives for.

Most importantly, the findings challenge the perception that the compulsory licensing derogation predominantly aids the most deserving countries. In fact, they suggest that least developed countries (LDC) are discriminated compared to developing countries with domestic manufacturing capabilities unintentionally. Since the WTO Doha Declaration in 2001 countries are allowed to export CL drugs to LDC without appropriate drug manufacturing capabilities. Our findings explain why such cross border compulsory licensing (CBCL) is virtually non-existent at the time.

All chapters of this thesis are connected and the findings from a preceding chapter feed the analysis in the following.

1.1. Structure and Literature

In order to draw the conclusion described above a first step is to outline the legal framework and assess compulsory licensing utilization in chapter 2. Subsequently, chapter 3 examines the static duopoly that unfolds from compulsory licensing to then look at dynamic aspects of patents in chapter 4 and price negotiations in chapter 5. For the pig picture chapter 6 analyses how the findings from chapters 3, 4 and

5 unfold in the context of an open economy. The conclusions are summarized in chapter 7.

Chapter 2 begins with a brief introduction to the evolution of international intellectual property legislation and outlines the patent relevant parts of the so called "TRIPS" agreement, implemented in 1995. The focus lies on the compulsory licensing instrument, with its scope expanded to cross border compulsory licensing (CBCL) by the Doha Declaration in 2001. A number of examples demonstrate how these compulsory licenses unfold in detail and the sole CBCL episode demonstrates how cumbersome the respective process is. A complemented and validated assessment of compulsory licensing by Beall and Kuhn (2012b) shows that between 2000 and 2012 a total number of 43 episodes occurred of which only five are related to low-income economies. These 43 episodes with an actual employment of 25 compulsory licenses oppose the perception that compulsory licensing is rarely used. However, low-income economies seem to flinch from using it, even though cross border compulsory licensing was introduced by the Doha Declaration. In particular the time consuming registration process as well as the requirement to early identify is described as aggravating even though it remains unclear why these prevent cross border compulsory licensing compared to domestic compulsory licensing.

In order to approach the question why low-income countries might be discriminated by the instrument of compulsory licensing a first step is to fade out any complexities related to dynamics or open economies, but to focus on the static closed economy impact of issuing compulsory licensing. Chapter 3 explains that in the resulting duopoly situation the innovator's quality advantage as well as the domestic generic manufacturer's distribution network advantage prevent pricing at production costs and allow both to keep profits. The analysis is substantiated by Chaudhuri, Goldberg, and Jia (2003) and Flynn, Hollis, and Palmedo (2009). A simplified model

based on Hotelling (1929) product differentiation also demonstrates how the leverage of these marketing advantages change in the socioeconomic properties of the drug's targeted indication. While for global diseases such as diabetes the innovator's quality advantage could partially prevent generic erosion, compulsory licensing for diseases that predominantly affect the poor population in rural areas will significantly expand access. With regard to remuneration section 3.3 demonstrates that for a majority of compulsory licenses a small royalty based on the generic's net sales was applied. Since this royalty is usually small the economic literature dismisses it as having a negligible effect on the generic's price. Yet, in the competition scenario the royalty's effect on generic prices might be amplified by the competition on top of the production costs.

In chapter 4 we discuss the dynamics of patent protection following Arrow (1962) and outline a number of inefficiencies in particular with regard to pharmaceutical research and development based on Tirole (1988), Scherer (2007) and Heller and Eisenberg (1998). The second part of chapter 4 provides an overview of selected alternatives and auxiliary mechanisms, namely Patent Buyouts (Kremer (1998)), Health Impact Fund (Hollis and Pogge (2008)) and Advanced Market Commitments (Kremer (2001)).

Subsequently, chapter 5 presents a negotiation game that demonstrates how the threat of compulsory licensing could reduce the innovator's pricing without employing it. This model also helps to understand that governments are especially likely to consider and issue compulsory licenses for drugs that target diseases predominantly affecting the poor population in rural areas. Neglected diseases accordingly suffer another uncertainty from the innovator's research allocation perspective. Most importantly, the model shows that a generic competitor will reduce pricing in the process of convincing the government of compulsory licensing if there are indirect

costs to it in the form of political pressure or the risk of jeopardizing foreign direct investment.

As chapter 6 explains this holds only for countries that have domestic generic manufacturers. Low-income economies dependent on drug imports do not have that price reducing advantage due to the cumbersome cross border compulsory licensing process. By opening the tedious application process for possible licensees these countries have already committed to compulsory licensing. Any indirect costs of issuing compulsory licensing vanish in the application process as they are sunk costs. The foreign generic competitor does not have to worry about undercutting a given threshold to convince the low-income economy of compulsory licensing. Further, the exporting country is obligated to issue compulsory licensing as well, which limits the number of eligible licensees, if any. Accordingly, the licensee will set the optimal duopoly price, which is either higher than or equals the price a domestic applicant would apply with. Additionally, cross border compulsory licensing involves transportation costs that add to production costs. Not only does this directly increase the licensees pricing, the effect of a royalty on the generic price will increase as well. Chapter 7 summarizes the results, discusses weaknesses of the analysis and suggests starting points for further research.

In the economic literature, among others, Kremer (2002) and Tirole (2006) address the access to medications in developing countries in a general way. Kremer (2002) gives the reader a broad outline of the problems impairing the supply of pharmaceuticals to the poor population. Among other subjects, he addresses the lack of research and development (R&D) coverage for neglected diseases and depicts policy options. Kremer (2001) also explores the idea of purchasing funds and goes into detail with the structure of purchase commitments and proposes a pricing mechanism. Tirole (2006) picks up the recent development in international intellectual

property rights, namely the TRIPS agreement and in particular the compulsory licensing instrument. His conclusions leave the reader with a pessimistic perspective. He criticizes, among other things, the lack of rules for issuing compulsory licensing and thus accompanies Kremer (2002) that "governments face free-rider problems in supplying the global public good of R&D and have time-inconsistent preferences regarding rewarding firms for doing so" (Kremer (2002), p. 69). There are many other contributions to the discussion on the question of how TRIPS will effect the accessibility to medications in developing countries. To name but a few Bird (2009), Reichman (2009) and Lybecker and Fowler (2009) evaluate the options from a legal perspective. Flynn, Hollis, and Palmedo (2009), Pradhan (2006), Grace (2004) and Lalitha (2009) analyze economic and welfare effects in a general way, but only few apply a quantitative approach. The market for essential drugs in developing countries was estimated by Goodman et al. (2009) and Chaudhuri, Goldberg, and Jia (2003), whereas the latter link it with TRIPS and simulate patent protection while not incorporating compulsory licensing. Importantly, Beall and Kuhn (2012b) conduct an analysis of media databases, assess numerous compulsory licensing episodes and challenge the perception that compulsory licensing is not used often. Kyle and McGahan (2011) analyze the investment in pharmaceuticals before and after TRIPS and find that the anticipated effect of higher R&D does not hold for countries with low income. With certainty this result is partly due to the low potential of developing countries to recoup high R&D. Although not considered by the authors, it is not so far off that the uncertainty induced by compulsory licensing ruins any remaining incentive for R&D as depicted by Tirole (2006). Kyle and McGahan (2011) suggest that alternative mechanisms to induce R&D for NDs are required.

1.2. Diseases Predominantly Affecting the Poor

A segmentation and categorization of diseases and drugs is difficult and can only be done with regard to specific questions. For example the Anatomical Therapeutic Chemical Classification System classifies drugs based on the organ or system targeted by the respective mechanisms of action as well as therapeutic or chemical characteristics. This system is controlled by the World Health Organization (WHO) Collaborating Center for Drug Statistics Methodology (WHOCC) and "recommended by the WHO for drug utilization studies" (WHOCC (2012), preface). In parallel, other systems such as the International Classification of Diseases, Classification of Functioning, Disability and Health or Classification of Health Interventions are utilized based on a problem setting at hand. While the above systems are very complex and consist of hundreds of subclasses other segmentations are more general and simplistic. For instance communicable, high burden, contagious or tropical diseases are segmentations serving distinct analytical questions and are based on different disease characteristics.

For the purpose of this work we look at the group of diseases for which relative to the burden of disease the private investment in research and development (R&D) is relatively low. We give this group an abstract definition in order to avoid confusion about time inconsistent and institutional diverse definitions for example with regard to neglected tropical diseases, also referred to as neglected infectious diseases. In reference to the low incentives we define the diseases lacking private investment as to affect predominantly the poor population in developing countries. While Human Immunodeficiency Virus (HIV), Malaria as well as tuberculosis are often not considered as neglected diseases due to considerable public investment we consider them as ND since "private investment as been far lower than might have been hoped, given the

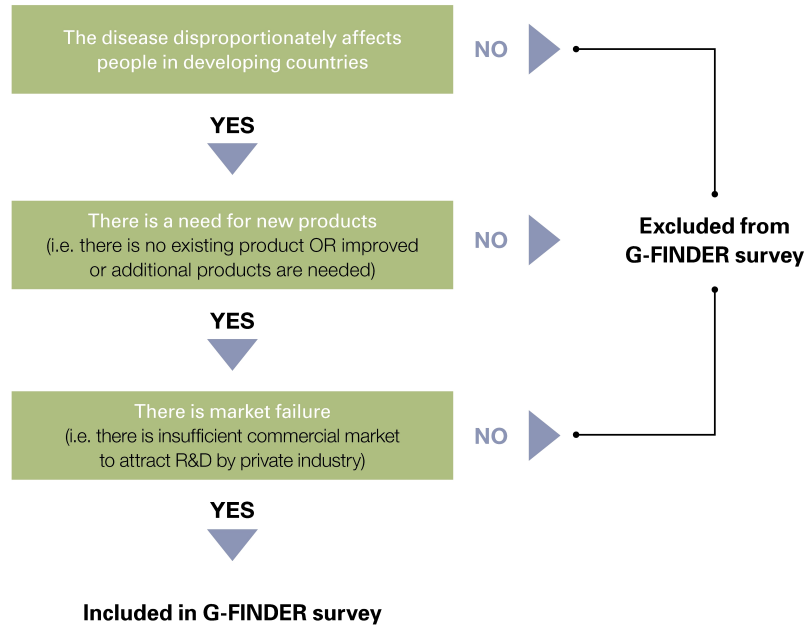


Figure 1.1.: Definition of neglected diseases as a filter applied in the G-Finder reports. Picture taken from Moran et al. (2012) p.14.

massive human toll of these diseases, particularly in the poorest countries” (citation from Batson and Ainsworth (2001)). While such a group is not often used in public or academic discussion it mirrors the organizational structure of the WHO. An important group in the WHO headquarters organizational structure is the ”HIV/AIDS, TB, Malaria and Neglected Tropical Diseases (HTM)” department, striving to increase investment and encourage new treatment solutions for the respective diseases. We henceforth refer to this group as the neglected diseases (ND). With this definition we follow rare economic literature such as Tirole (2006) as well as the so called G-Finder surveys. These Reports are sponsored by the ”Bill & Melinda Gates Foundation”, namely the report on *Neglected Disease Research and Development: A Five Year Review* (Moran et al. (2012)) and taken on by the *Global Report for Research on Infectious Diseases of Poverty* (World Health Organization (2012)). Figure 1.1 depicts the concept of which diseases are included in the group of ND.

The resulting 31 NDs can be split into 3 tiers according to their relative funding. While the top tier group consisting of HIV/AIDS, tuberculosis and malaria each received approximately one-third to one-fifth of total ND funding in 2010 (figure 1.2), the third tier diseases each received less than 0.5%.

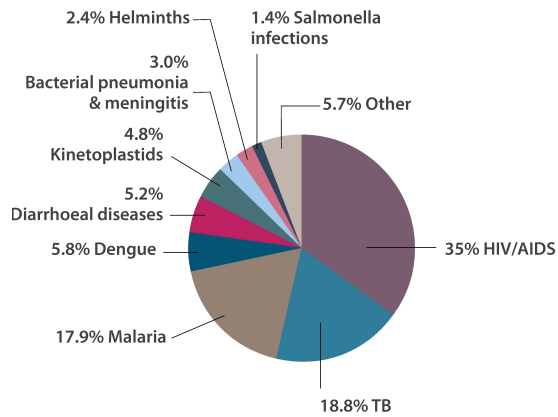


Figure 1.2.: Allocations of R&D for neglected diseases 2010 from World Health Organization (2012), p.131.

By 2011 64% of global NDs R&D funding came from the public sector, 19% from philanthropic contributors and 17% from pharmaceutical industry (Moran et

al. (2012) p. 11). The research funding from the pharmaceutical industry is entirely internal (intramural) meaning that the developed drugs are potentially under patent protection (World Health Organization (2012), p 128). Moran et al. (2012) report a decreasing trend for public and philanthropic funding following the global financial crisis while private investments increased dramatically, yet mainly allocated in trials for dengue vaccines. Further, the survey identifies a trend of decreasing investment in the top tier diseases and increasing investment in second tier over five years as figure 1.3 demonstrates.

The Human Immunodeficiency Virus (HIV) causes the Acquired Immune Deficiency Syndrome (AIDS) and is mainly transmitted via sexual interaction, injection of drugs or children infected by their mother's blood. The *UNAIDS Report on the global AIDS epidemic 2012* (United Nations Programme on HIV/AIDS (2012)) reports a steady decline in new infections globally while at the same time more than 60% of people infected with HIV received life saving treatment which reduced the death due to

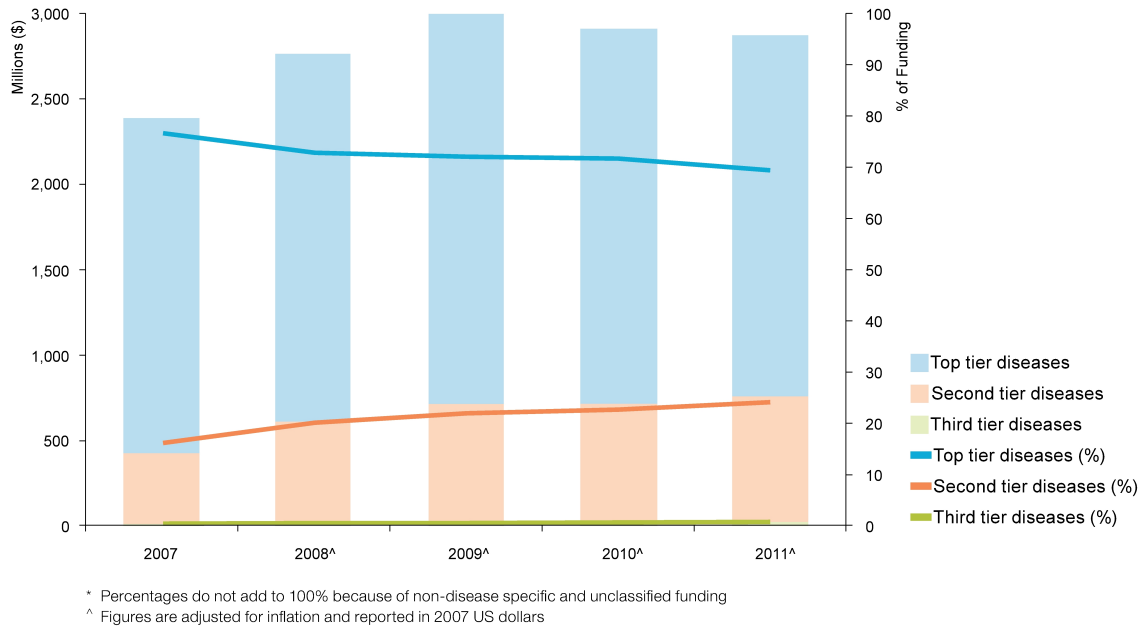


Figure 1.3.: Neglected diseases funding development by tiers. Graph taken from Moran et al. (2012). p.25.

aids significantly between 2000 and 2011.

While Moran et al. (2012) report that an effective vaccine against HIV/AIDS is still many years away due to rapid virus mutation, combinations of antiretroviral (ARV) medication are administered to decrease the probability of AIDS progression and risk of death. However, even these require additional R&D as they are not adapted to the need of developing countries, "for instance, paediatric formulations and fixed-dose combinations are needed" (Moran et al. (2012), p. 26). While research funding for HIV/AIDS is highest among all neglected diseases, this is the case due to significant public donations only. Only a small portion of it comes from private R&D investments. Additionally, figure 1.4 shows that HIV/AIDS funding decreases since 2008.

If not treated malaria can lead to death especially for pregnant woman and young children. The severe form plasmodium falciparum is most effectively treated with

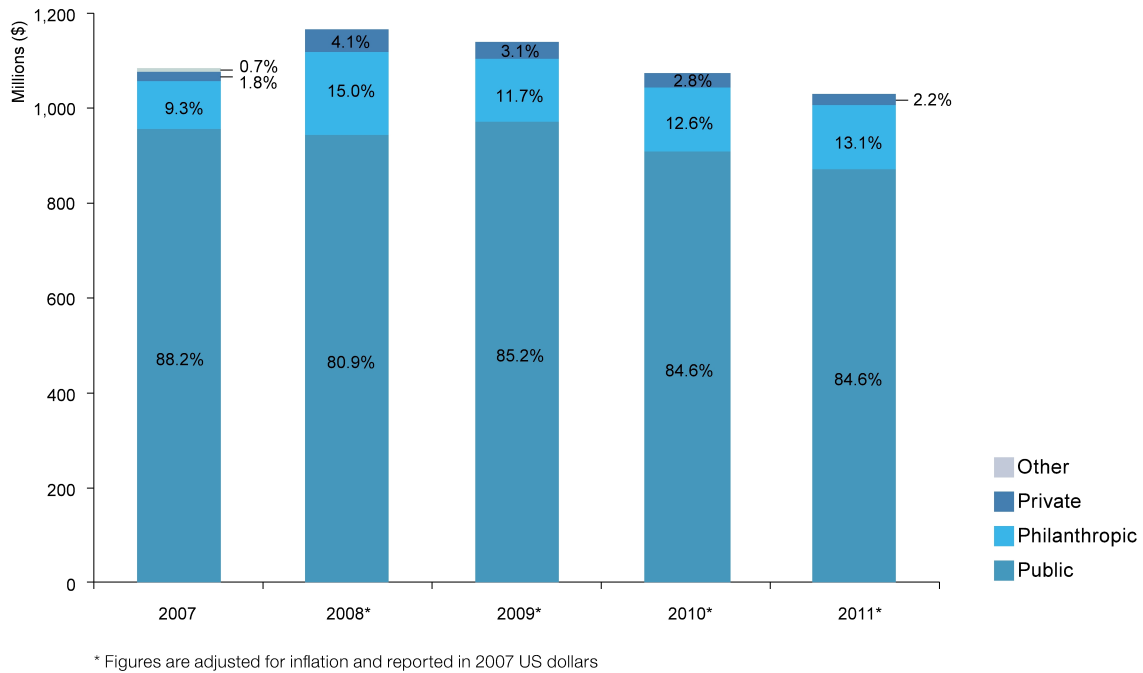


Figure 1.4.: HIV/AIDS R&D funding by funder types 2007-2011. Graph from Moran et al. (2012). p.25.

so called artemisinins. In the standard therapy these are combined with other anti malaria compounds to reduce the risk of the virus to develop a resistance to the single drug. However, emerging virus resistances to this artemisinin-combination therapy as well as mosquito insecticides used for vector control require further R&D efforts (Moran et al. (2012), p. 30). A glimmer of hope emerges due to a vaccine candidate already in phase III trials RTS,S to cut the risk malaria infection in half.

The bacterial infectious disease tuberculosis affects predominantly the lung and is in particular lethal for patients infected with HIV/AIDs. Current treatment requires the administration of multiple drugs over up to 24 month often co-administered with ARV therapies. The resulting low compliance and emerging drug resistances highlight the high need for new drugs to be efficient, quicker and simpler in treatment as well as safely co-administered with ARV therapies fighting HIV/AIDs. Additionally,

there is a strong need for cheap, rapid, accurate and easy diagnostics tailored for the needs of developing countries as well as a new vaccine to displace an outdated one (Moran et al. (2012), pp. 34).

Dengue fever transmitted by mosquitoes and in particular dangerous for children. Currently there is neither a curative drug nor a preventive vaccine available. Dengue differs from other neglected diseases since it has at least some commercial value for private investors to develop drugs for travelers, military and mid-income countries in Asia and South America as figure 1.5 demonstrates (Moran et al. (2012), p. 39).

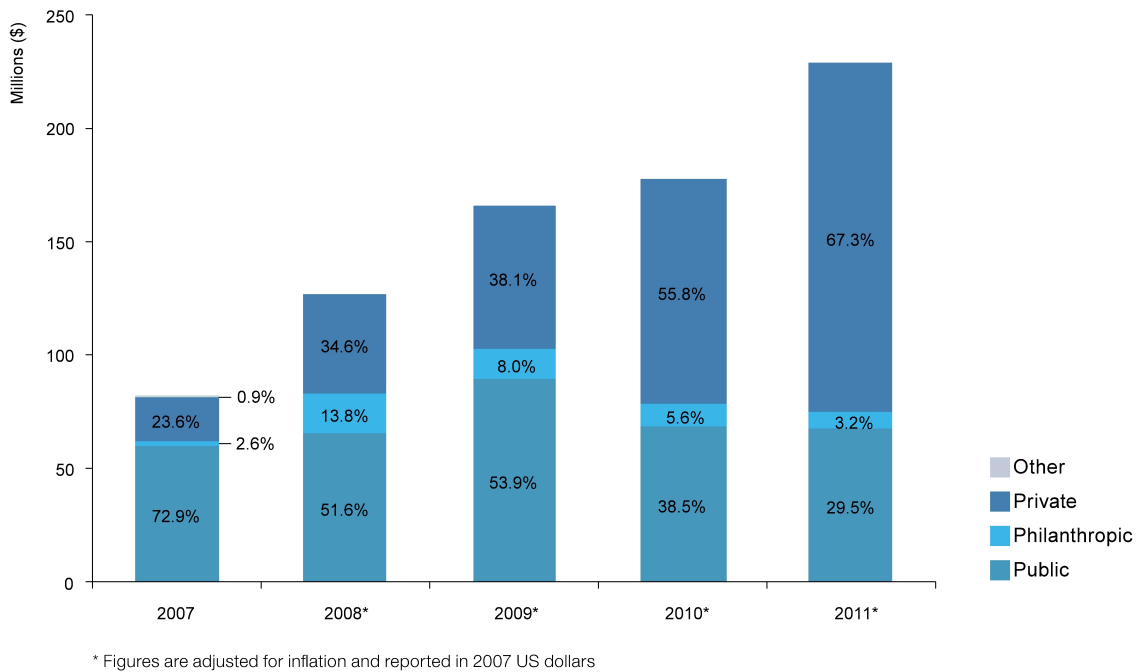


Figure 1.5.: Dengue R&D funding by funder types 2007-2011. Graph from Moran et al. (2012). p.42.

While there are 27 more diseases all of these require additional R&D efforts either in general or to tailor treatment for developing countries. These diseases are neglected since they do not motivate enough R&D from private investors in relation to the burden of disease and affect mainly the poor population. Chapter 4 briefly outlines how expected return of investments as induced by a patent system incentivizes inno-

vation. The expected revenue from selling a medication for a ND is not high enough to motivate large R&D cost.

The World Health Organization (WHO) stated in 2001, that there is "substantial level of R&D activity underway" for several infectious diseases (World Health Organization and International Federation of Pharmaceutical Manufacturers and Associations (2001) p. 1.), especially malaria and tuberculosis. By 2010 the situation has improved slightly and the WHO's goal with regard to ND shifted towards increasing the production of generic pharmaceuticals. However, more research for new medicines remains an important factor as the above examples explain. Additionally, existing medications require alternations and improvements to meet the needs in developing countries. For some diseases accessibility and treatment is very difficult due to serious side effects or the need of multiple administrations (World Health Organization and International Federation of Pharmaceutical Manufacturers and Associations (2001) pp. 7-8). The underdeveloped infrastructure of developing countries hinders an effective distribution of essential drugs. For example, the second line antiretroviral Kaletra by Abbott is such an improvement especially suited for developing countries. Contrary to its earlier version it does not "require refrigeration" or has to be taken with food. Such improvements can also be considered as "neglected" and especially for vaccines this proves to be a serious problem (Charlish (2011) p. 19).

The compulsory licensing episodes depicted in the coming chapter 2 mainly concern HIV/AIDS medications, that is to say several antiretroviral drugs.

2. TRIPS Agreement and Flexibilities

All beginnings are difficult and it is vital to challenge and review information as a first step of research. All too often the literature perceives the so called compulsory licensing as a neglected instrument. This chapter demonstrates that in fact it is frequently used and points out that cross border compulsory licensing is the critical element to be investigated. Auxiliary, we outline global patent protection and detail the evolution as well as selected applications of compulsory licensing. Before turning towards the economical static, dynamic and open economy aspects of compulsory licensing it is important to explore the context of this instrument.

Intellectual property rights (IPR) are an abstract concept. They do not apply to concrete objects but aim to reward an intellectual creation and express moral acknowledgment. According to the World Intellectual Property Organization (2004) the two branches of "industrial property" and "copyright" are distinguished traditionally. While the latter covers literary, artistic and scientific works, industrial property envelopes industrial designs, trademarks and inventions. These inventions can be described as a new solution to a specific technical problem and are subject to requirements such as applicability as well as novelty. They are acknowledged by means of patents in an IPR framework. Essentially, a patent is a document proving the government's recognition, describing it in an disclosed way and, most impor-

tantly, implying rights. It does not approve the exploration of the invention but represents what is called the "right to exclude" others from doing so. Such disclosure of others and the right to enforce it constitutes a patent and is limited to a period.

This chapter will begin by briefly touching the evolution of globally harmonized IPRs and subsequently outline the legal situation and implementation to date. The key aspects examined here are international patent protection as well as flexibility in form of the compulsory licensing (CL) instrument. We focus on assessing the utilization of compulsory licensing in the second part of this chapter and describe several key compulsory licensing episode examples.

In conclusion, all WTO member countries are allowed to license a generic manufacturer without the right holders approval even though the respective product is under patent protection. Investigating multiple compulsory licensing episodes shows that price negotiations lead to discounts rather than compulsory licensing for several of these episodes. A novel assessment of CL episodes by Beall and Kuhn (2012b) is depicted and confirmed by several individual sources per episode. In particular, this proves wrong a widely spread perception in literature of rare compulsory licensing usage. Cross border compulsory licensing on the other hand is not popular and the question remains why in detail this is the case. In order to shed light on this question the findings of this chapter serve as a base for argumentation of the upcoming analysis.

2.1. From Paris Convention to TRIPs

The origins of patent protection are difficult to determine as some regulations might not have followed the intention to increase incentives for innovation. Khan (2006) provides a comprehensive summary of the history of patents and explains how they developed from the guild system in Europe. While at a later date British monarchs frequently rewarded minions by granting patents, the Republic of Venice is considered to having established the first patent legislation. Only in the seventeenth century patents became associated with incentives entirely, even though initially restricted by high fees. The ”‘*WIPO intellectual property handbook: policy, law and use*’” (World Intellectual Property Organization (2004)) details the origins of the modern IPRs. Following Britain, other countries such as France and Germany implemented a patent system in the late eighteenth century, having awarded inventors directly before. The United States also passed a patent statute in the late eighteenth century, but with greater success than other countries. The implemented patent system was modern and explicitly intended to promote economic growth and social welfare.

As more and more countries installed IPRs it became clear that an international harmonization is needed. Obtaining protection for an invention in several countries was difficult due to the diversity of systems and rules. Additionally, a delayed application in one country after a publication in another put the recognition of novelty at risk. The lag of international harmonization became apparent as an exhibition of inventions in Vienna took place in 1873: Inventors hesitated to exhibit their innovation out of fear to lose the status of novelty in other countries. During the same year the Congress of Vienna for Patent Reform laid the foundation for international negotiations to harmonize IPR which resulted in the Paris Convention treaty ten years later (World Intellectual Property Organization 1883).

In order to overcome this diversity the Paris Convention specified rules to harmonize national IP legislation and in particular the "national treatment" provision enforced equal treatment of other member country's nationals. Further, the "right of priority" regulates that a delayed application within a given time frame will be handled as if it happened the same day as the earliest application among the member states. Belgium, Brazil, El Salvador, France, Guatemala, Italy, the Netherlands, Portugal, Serbia, Spain and Switzerland signed the agreement, even though the so called "patent controversy" imperiled and interrupted patent protection in some European countries. Whilst the Paris Convention covers the "industrial property", in 1886 another treaty introduced a similar harmonization on copyright, known as the "Berne Convention for the Protection of Literary and Artistic Works".

The number of signers for both treaties grew over time and was in particular boosted after World War II. As to date, the Paris and Bern Conventions are still in force and originated a new and broader framework established in the 20th century. This agreement of "Trade-Related Aspects of Intellectual Property Rights" (TRIPs, World Trade Organization 1994) even cites the Paris and Bern Conventions while not annulling them. It resulted from the Uruguay Round under the "General Agreement of Trades and Tariffs" (GATT), which installed the World Trade Organization (WTO). The "Uruguay Round" refers to the eighth GATT round, which was launched in September 1986 in Punta del Este, Uruguay and finished on April 15, 1994 in Marrakesh, Morocco. It also had other objectives, for instance to reduce agricultural subsidies and to open service trades. The "Trade Related Investment Measures", "General Agreement on Trade and Services", "Multilateral Agreements on Trade in Goods" are the main outcomes of the negotiations, apart from the TRIPS agreement. These agreements are ratified as an annex of the WTO agreement and came into effect on January, 1st 1995.

TRIPs bounds all WTO members to minimum IPR standards and regulates the dispute settlement of infringement as WTO jurisdiction (World Trade Organization 2006). The minimum patent protection in accordance with TRIPS numbers 20 years for any invention and is granted for products as well as processes. In accordance with the Paris Convention these are subject to three criteria regulated in article 27 of TRIPS, namely novelty, newness and industrial applicability. The exclusivity granted refers to "marketing, using, offering for sale, selling, and importing" a product (World Trade Organization 1994, article 28), regardless of the field of technology, place of invention or whether the product is locally produced or imported (World Trade Organization 1994, article 27). This also demonstrates the adoption of former GATT non-discrimination legislation in TRIPS. Countries that join the WTO after the TRIPS Agreement are obliged to have implemented TRIPS by the beginning of their membership (World Trade Organization 2001, page 7). For member countries, the WTO differentiates between developed, developing and least developed countries when it comes to the schedules of implementing TRIPS. Whereas developed countries had one year to incorporate the TRIPS rules into their legislation after the ratification in 1995, developing countries were given until the year 2000. For least developed countries, the original time-line of 2006 was extended until 2016 with regard to pharmaceuticals by the Doha conference (World Trade Organization (2001), paragraph 7. and section 2.3).

Probably the most controversially discussed component in the TRIPS agreement is the flexibility granted in view of developing countries.

2.2. Compulsory Licensing

While enhancing patent protection on the one side, the TRIPS agreement also strives for a balance regarding emergencies and access to essential medicines on the other. Thus, article 31 concedes an instrument to members allowing "other use without authorization of the right holder", which is typically addressed to as "compulsory licensing" (CL), although it additionally envelops government usage (World Trade Organization 1994, article 31, see appendix A.3). CL is traditionally incorporated into international IP treaties as a loophole in case of patent abuse or if the patent is not worked sufficiently as well as generally to support public interests. The Paris Convention also allows for compulsory licensing in Article 5A with regard to these reasons (World Intellectual Property Organization 1883). Within the TRIPs framework the legitimacy conditions of using CL are that

1. the licensee has made efforts to obtain authorization from the patent holder,
2. the duration of the licensing is limited,
3. no exclusiveness to licensee is given,
4. product is used for supply of the domestic market and
5. an adequate remuneration is paid.

Out of these, the first condition can be waived "in the case of a national emergency or other circumstances of extreme urgency or in cases of public non-commercial use", and is together with the fourth non-mandatory if a judicial process determines anticompetitive practice (World Trade Organization 1994, article 31 b and article 31 k). The determination of an adequate remuneration as well as the a national emergency lies in the judgment of nations utilizing the instrument.

In order to investigate some examples of compulsory licenses, it is reasonable to distinguish between two types, domestic compulsory licensing and cross border compulsory licensing (CBCL). Some few developing and middle income countries possess a pharmaceutical industry capable of producing the respective drugs. Others, especially least developing countries, are less capable of domestic production so that the desired drugs have to be imported.

2.2.1. Compulsory Licensing under Domestic Production

The following will depict examples of compulsory licensing episodes of developing countries capable of producing the licensed drugs domestically. In general, issuing of compulsory licensing is very controversial and preceded by negotiations between government, generic petitioner and innovator. In order to underline the intensity of compulsory licensing disputes the case of South Africa in 1997 is showcased first. The South African controversy gained much attention internationally and especially shifted the political attitude with regard to TRIPs flexibilities globally as Fisher III and Rigamonti (2005) summarize. Thereafter, episodes in Brazil and India throw a light on exemplary processes and time lines.

South Africa considered the idea of compulsory licensing already in 1997 by introducing the "Medicines and Related Substances Control Amendment" (MRSCA) Act No. 90 (South Africa (1997)). The Acquired Immune Deficiency Syndrome (AIDS) epidemic was rampant in South Africa with an adult prevalence rate of almost 20%. Between the emerge of AIDS in 1981, the discovery of the "Human Immunodeficiency Virus" HIV in 1984 and the first democratic elections in South Africa in 1994, the disease spread almost unhindered. The health care system was extremely unequal,

with approximately 80%, mostly native South Africans, relying only on public health care.

The antiretroviral drugs (ARV) available were still patented and like today did not cure but decelerate the process of AIDS. As South Africa became TRIPS compliant in 1997 with the Patents Act this treatment became very costly. The post-apartheid government under Nelson Mandela struggled with this AIDS crisis and the MRSCA was meant to relief the budgets by generic substitution, parallel imports, transparent and controlled pricing as well as clearing the way for cross border compulsory licensing (CBCL). The international pharmaceutical industry feared that other developing countries might follow the South African model and 40 innovators filed a lawsuit, challenging the MRSCA constitutionally. The U.S. Clinton administration as well as the European Union additionally imposed pressure against the MRSCA. The United States trade representatives pursued a so called TRIPS plus policy, which adheres to a tighter standard than agreed in TRIPS as Ford (2000) explains. Initially, the focus of South Africa was not on compulsory licensing but on price reduction via transparent pricing and parallel imports, in article 15C in MRSCA (South Africa (1997)). The controversy evolved around the interpretation of TRIPs and the U.S. ambition to push TRIPS plus. Compulsory licensing was brought to the forefront in the process of the international public and political debate.

A lawsuit filed by the pharmaceutical Industry turned out to be a disaster. The international public opinion strongly supported the South African matter and innovators suffered a major and lasting damage to their public image. The U.S. as well as E.U. administration withdrew the political pressure in 1999 and one by one the companies abandoned the action. The Secretary General of the United Nations, Kofi Annan, was asked by GlaxoSmithKline's president Jean-Pierre Garnier to resolve the matter with Thabo Mbeki, at the time president of South Africa. In April

2001 the lawsuit was settled and the MRSCA came into effect. Additionally, several alliances fighting AIDS were founded such as the "Accelerating Access Initiative". Apart from institutions like WHO and UNAIDS some international pharmaceutical corporations joined these initiatives and provided cheap antiretrovirals (ARV), perhaps to limit the damage to public relations. Further, the Global Fund to fight HIV/AIDS, tuberculosis, and malaria was established by Governments and Non-Governmental Organizations (NGOs), motivated by the U.N.. However, a request for voluntary licensing of ARVs by South African generic manufacturers remained unanswered, apart from a single license to Aspen Pharmacare with 15%-30% royalties. As a reaction an investigation of pricing practices was filed with the South African Competition Tribunal against GlaxoSmithKline and Boehringer Ingelheim in September 2002 (World Health Organization 2008, page 4). Additionally, the Indian generics manufacturer CIPLA officially requested CL for 8 ARVs, increasing the pressure on innovators. The case was settled in April 2003 and the two companies allowed several generic companies to produce and distribute their ARVs in the sub-Saharan African Region for 5% royalties. Subsequently, some manufacturers such as Boehringer Ingelheim or Roche have granted a non-assert declaration. Such confirm that the innovator will not enforce existing patents on their ARVs in certain regions and as a result not receive any royalties.

Brazil publicly considered to issue a CL on Merck Sharp and Dohme's (MSD) drug Efavirenz in 2001, according to Wetzler and Ayala (2008) and Beall and Kuhn (2012b). As a result of the threat and negotiations, MSD agreed to give a discount of 59% as well as 65% on Indinavir, a protease inhibitor also used for the treatment of HIV. Brazil additionally negotiated with Roche about a CL on their ARVs Nelfinavir and succeeded in getting a 40% discount the same year. Other negotiations went

on for a couple of years, but eventually agreements on reduced prices were signed. Bristol-Myers Squibb, Gilead and Abbott also agreed on major discounts after being threatened with CL.

In 2007 Brazil issued a compulsory licensing to FarManguinhos, an entity of the Oswaldo Cruz Foundation of the Government of Brazil, for Efavirenz. The CL was used because MSD refused to price at the same level as it did after the CL negotiations in Thailand, which is described in the next sub section. The Brazil government set the royalty to 1.5% even though it was recommended by activists to use the 2005 WHO/UNDP remuneration guidelines, or establishing a prize fund (Love (2007)). These guidelines are further depicted in the Ecuador case of compulsory licensing below, as they were employed here. However, FarManguinhos was unable to produce medication for two years due to a lag of technological knowledge and temporarily Indian manufacturers stepped into the breach.

India issued a compulsory licensing on the cancer drug Nexavar in March 2012. In contrast to other CL episodes this decision is well documented (Government of India (2012)). The respective substance Sorafenib is used for advanced liver as well as kidney cancer and extends the expectation of life by four to eight years. It was patented and launched by Bayer corporation in India by 2008. The applicant for compulsory licensing, Natco Pharma Limited, offered to sell the drug at a price of Rs 8,800 (\$ 180) of monthly treatment costs compared to Rs 280,428 (\$ 5,600) of the original product by Bayer. An interesting factor in this situation is that another Indian generic manufacturer, Cipla Limited, already sold Sorafenib at monthly costs of Rs 30,000 (\$600) since May 2010. But as Bayer filed a patent infringement suit and did import Nexavar in inadequate quantities, the compulsory licensing was issued.¹

¹Note that India is a member of the Paris Convention since 1998, which might be more strict with regard to CL in certain cases. The reason for CL usage here is that Bayer did not "sufficiently

With the decision, the applicants price is fixed at a maximum of Rs 8,880 monthly treatment for the respective indications and Natco is obliged to donate Sorafenig to 600 needy patients each year. On the pricing side, the Government of India (2012) follows the applicants proposal but adds the element of obligatory charity. The royalty rate is set at 6% of Natco's sales and the license is non assignable. Further, the sold product should not be associated with Nexavar and thus has to be sufficiently distinct.

It is crucial to note some sequels of this decision: Initially, Natco expected sales of five to six million U.S. dollar, according to a statement by Natco's finance chief, Baskara Narayana (Reuters (2012a)). The other Indian manufacturer Cipla, which faces an infringement lawsuit by Bayer, cut the price of its Sorafenig. Cipla priced at 6,840 rupees (\$130), thus undercutting even Natco Pharma with Rs 8,800 (\$180) (Reuters (2012b)). For the duration of Bayer's patent infringement suit against Cipla this price cut will have major impact on Natco's sales. Especially since in India the domestic competitor's rate of substitution is higher than with a multinational company, according to Chaudhuri, Goldberg, and Jia (2003). Another reaction could be interpreted as a precautional action: Roche announced to cut prices of 2 cancer drugs by 2013, Herceptin and Mabthera. In order to avoid parallel trade these products will also be renamed.

2.2.2. Import Compulsory Licenses

Some countries are not able to produce the desired drugs domestically and have to rely on imports. However, the CL provision in TRIPS initially required the licensed

work" the patent for which CL may not be requested before three years have elapsed after the patent was granted. Since Nexavar was patented in India by 2008 this criteria is met. See World Intellectual Property Organization (1883), article 5A.

product to be used for supply of the domestic market only. In other words no TRIPS compliant country was allowed to supply the required drugs under patent, even if issuing a compulsory license themselves. Later, the Doha declaration included an amendment which waived the requirement of domestic supply. These we specify as cross border compulsory licensing (CBCL) since importing and exporting country are required to issue CL.

Before introducing CBCL in the next section 2.3, the following will go into detail with CL via export from India. India became TRIPS compliant with the Indian Patent Act Amendment in 2005 (Government of India (2005)). Nonetheless, no compulsory licensing in India was required initially: The Indian patent act regulates that "enterprises which have made significant investment and were producing and marketing the concerned product prior to the 1st day of January, 2005" cannot be subject to infringement proceedings (Government of India (2005), amendment of section 11A, paragraph 10c). Thus, India acts as a pharmacy for the third world, especially with regard to compulsory licensing. We denote these events as import compulsory licenses (ICL) and differentiate them from domestic compulsory licensing (DCL) or cross border compulsory licensing (CBCL)

Thailand announced it's plan to issue a CL for MSD's HIV drug Efavirenz in November 2006 in order to have a better position for negotiations (Wetzler and Palmedo (2008), Khor (2010), Beall and Kuhn (2012b)).

This CL without prior negotiation with the patent holder was subject to international and domestic criticism but also found numerous support with NGO's. A royalty fee of 0.5% of the generics total sales was granted to MSD and distribution as well as production of the generic drug was conducted by the Government Pharmaceutical

Organization (GPO). It turned out that GPO was not able to produce the drug in the desired quality. Even though the Global Fund to Fight HIV/AIDS financially supported the improvement of production facilities, GPO failed in securing quality of its product. Till now, the supply of drugs is secured by a diversity of Indian drug manufacturers.

MSD decreased its price to a level just under GPO's but nonetheless, the Thailand's government adheres to the CL in order to create a precedent for a CL of other diseases. Accordingly, Thailand issued additional compulsory licenses in 2007 on another antiretroviral (ARV) drug Kaletra (combination of Lopinavir & Ritonavir) from Abbott as well as on Sanofi-Aventis against hypertension. The latter has been the first time that a developing country issued a compulsory licensing for a non ARV. Prior to this, price reductions of the innovators for all developing countries did not convince the Thailand government refrain from CL. As a reaction, Abbott withdrew all its products from Thailand and planned not to introduce new medications. The WHO pointed out that Thailand should improve its relationship with innovative pharmaceutical companies as Kyle and McGahan (2011) depicts. Further, the cancer drugs letrozole (Novartis), docetaxel (Sanofi-Aventis) and erlotinib (Roche) compulsory licensed shortly after.

Novartis avoided a CL for Imatinib (Glivec) with the drastic decision to supply the drug for free to households with income per year of less than 1.7 million baht via the Glivec International Patient Assistance Programme-GIPAP.

Ecuador issued a CL in April 2010 according to Saez (2010). The drug is manufactured in India by the generic company Cipla and distributed within Ecuador by Eske Group SA. The licensed drug is an ARV from Abbott Laboratories, ritonavir,

and will be licensed until the end of patent in November 2014. Ecuador determined the royalty by the "Remuneration Guidelines" for Non-Voluntary Use of a Patent on Medical Technologies (Love (2005)), which are recommended by the WHO. The royalty structure differs from the regular CL royalties as it is not based on the generics price in the licensing country, but the innovator's price in a high income country. Additionally the royalty is tiered, accounting for the income per capita. The so called "Tiered Royalty Method" is further discussed in section 3.3.

2.3. Doha Declaration

The importance of the TRIPS Agreement for public health in developing countries was stressed by the WTO ministerial conference in Doha in 2001. With the Doha declaration the WTO members stated to strike a balance between short term access and long term incentives. Furthermore, an extended transition period with regard to pharmaceutical patents for least developed countries until 2016 was agreed on (World Trade Organization (2001) paragraphs 1-4). Developing countries other than least developed countries had to adapt the TRIPS regulations in domestic law until 2000. Developed countries were obliged to adjust their legislation within a year if not already in line with TRIPS (World Trade Organization (2001), page 7).

Most importantly, the ministers assigned the WTO to grant more flexibility to developing countries without the infrastructure to produce drugs on its own in light of the fourth topic of the conditions for compulsory licensing. The WTO waives this condition by which is usually referred to as the Doha Declaration's paragraph 6 decision (World Trade Organization (2001), paragraph 6). Further, the WTO regulates that remuneration should only be paid by the exporter. The waiver is planned to

be replaced by a TRIPS amendment, approved by WTO members in 2005 during the Hong Kong ministerial conference, but the required two thirds of the WTO members have not yet accepted to date. The Doha round is still an ongoing negotiation also with regard to agriculture (World Trade Organization (2005), paragraph 40).

If a developing country is not capable of producing a drug itself, compulsory licensing can only work if the respective drug is imported. Many countries have implemented the possibility of CL for export in their legislation but the upcoming will go into detail with the only country that so far exported via CL: Canada.

Canada & Rwanda worked the first and only compulsory licensing so far under paragraph 6 in 2008 for the HIV antiretroviral triple combination Zidovudine, Lamivudine and Nevirapine. Prior to this, Canada implemented the "Access to Medicines" Regime (CAMR) in 2005 intending to supply medicines for developing countries that issue a compulsory licensing and lack the production infrastructure. CAMR is based on the WTO decision that drugs under compulsory licensing can be imported from another country as regulated by the Doha declaration's paragraph 6. This regime served as a prototype for several equivalent legislations for example in the EU or USA (Government of Canada (2006) Annex B). The CAMP presentation (Government of Canada (2011)) as well as the governmental consultancy paper (Government of Canada (2006)) give a comprehensive overview on the features and history for the CAM regime. It shows, that under paragraph 6 and CAMR the following rules apply:

1. Importing generics from another country requires of both countries, exporting and importing, to issue a compulsory licensing (World Trade Organization (2003), paragraph 6).
2. CL is restricted to drugs that are listed by the WHO as essential medicines.
3. The exported products from Canada have to meet Canadian requirements in

terms of safety, effectiveness and quality.

4. It has to be ensured that the products can be distinguished from those in the Canadian market by coloring and labeling.
5. The exporting Canadian company is bound to pay the fees related to the regulatory process.
6. A patent holder can challenge the compulsory license when the exported generic's price exceeds 25% of the Canadian original drug price. Other measures make sure that the process is as transparent as possible.
7. The duration for the compulsory licensing is limited to 2 years.
8. Royalty rate is defined by a formula and is to be paid by the exporter.
9. The generics manufacturer has to quantify a maximum number of goods for export.
10. A supply agreement with the importing country has to be concluded. This agreement has to be in place before the application for compulsory licensing prior Health Canadas Drug Review (Government of Canada (2006) pages 6-7).

Whereas the first points are straight forward and might not surprise, the requirements 8, 9 and 10 caused some discussion and need further review.

The royalty fee is to be paid in percentage of the "monetary value of the supply contract" and is linked to the "UN Human Development Index" so that "the lowest country on the index has to pay a royalty of approximately 0.02 percent, and the highest 3.5 percent" (Government of Canada (2006), page 8.) This approach has been supported by NGOs and meets the WTO TRIPS amendment to take "into account the economic value to the importing member" (World Trade Organization (2010), paragraph 3).

In order to meet condition 9, the generic manufacturer needs to know the quantity requirements, which proved to be especially difficult with regard to developing countries. The drug manufacturer, Gilead, expressed to have had difficulties determining future needs which is a basic criteria for compulsory licensing (Weber and Mills (2010), page 115). The manufacturer is additionally obliged to have an agreement in place before the compulsory licensing application. This causes a dilemma as the developing county cannot enter an agreement without knowing that the manufacturer can deliver.

The first company using the "paragraph 6 decision" on on domestic supply worldwide was the Canadian generics company Apotex Inc., utilizing CAMR. Apotex won Rwanda's tender for the HIV antiretroviral triple combination Zidovudine, Lamivudine and Nevirapine with the name "Apo TriAvir" and shipped it in 2008 as Apotex (2008) reports. This tender was only a charade as Apotex was the only bidder. Apart from the above depicted requirements, which are cost intensive and time consuming, Apotex experienced that the greatest difficulty was to encourage developing countries to self-identify. Weber and Mills (2010) explain that developing countries stated that due to pressure from innovators and the world bank, they do not wish to self identify at an early stage. Additionally, developed nations try to influence the decision making in developpeing countries. With regard to the Ecuador case depicted below Wikileaks published an evadable leaked cable which shows that U.S. tried and failed to organize against Ecuador compulsory licensing (Wikileaks (2009), *Cable 09QUITO998*).

Weber and Mills (2010) argue that the Apotex shipment to Rwanda would remain the only use of paragraph 6 if not "simplified and streamlined" as it was "a result of factors whose conjunction will not likely be repeated"(Weber and Mills (2010), page 118-119). It was feared generally, that the Apotex case remained the only com-

pulsory licensing making use of the paragraph 6 provision as the obstacles described above seemed too strong (e.g. Kyle and McGahan (2011), Chami and Wasswa-Kintu (2011)). The matchmaking as well as legal processes for the importing country were heavily assisted by Médecins Sans Frontières (MSF), the Clinton Foundation and the Canadian regulatory authorities. More importantly, it was argued that the early commitment of Apotex as well as the willingness of Rwanda to use compulsory licensing were necessary conditions for the one-time success.

Having described some exemplary compulsory licenses the next section will provide a non-exclusive summary of compulsory licensing episodes, which will serve as a base for discussion.

2.4. Utilization Assessment

Apart from the compulsory licenses depicted above there are more countries with a compulsory licensing history. Before Beall and Kuhn (2012b) published the first peer reviewed research on compulsory licensing episodes the literature was divided on judging their number. Beall and Kuhn (2012b) methodically combed through several media, academic, and legal databases by using the phrase "(pharma! OR drug) AND (compulsory licen!)". Their findings serve as a basis for table A.1, augmented from various sources.

CHAPTER 2. TRIPS AGREEMENT AND FLEXIBILITIES

Row	Episode Period	Nation	Population ^k in mio.	National Income Group ^l	Desease Group	Molecule	Outcome	Sources
1	2001	Brazil	195	UMIE	HIV/AIDS	efavirenz	Discount	a c
2	2001	Brazil	195	UMIE	HIV/AIDS	indinavir	Discount	c
3	2001	Brazil	195	UMIE	HIV/AIDS	nefinavir	Discount	a c
4	2002	Zimbabwe	13	LIE	HIV/AIDS	all	CL	a
5	2002	Egypt	81	LMIE	NCD	sildenafil	CL	a
6	2003	Brazil	195	UMIE	HIV/AIDS	atanazavir	Discount	a c
7	2003	Malaysia	28	UMIE	HIV/AIDS	lamivudine	CL	a j m
8	2003	Malaysia	28	UMIE	HIV/AIDS	didanosine	CL	a j m
9	2003	Malaysia	28	UMIE	HIV/AIDS	zidovudine	CL	a j m
10	2003	South Africa	50	UMIE	HIV/AIDS	lamivudine	VL	a
11	2003	South Africa	50	UMIE	HIV/AIDS	nevirapine	VL	a
12	2003	South Africa	50	UMIE	HIV/AIDS	zidovudine	Discount	a
13	2003	South Africa	50	UMIE	HIV/AIDS	stavudine	Discount	a
14	2003	South Africa	50	UMIE	HIV/AIDS	didanosine	Discount	a
15	2003	South Africa	50	UMIE	HIV/AIDS	efavirenz	Discount	a
16	2003	South Africa	50	UMIE	HIV/AIDS	indinavir	Discount	a
17	2003	South Africa	50	UMIE	HIV/AIDS	abacavir	Discount	a
18	2004	Mozambique	23	LIE	HIV/AIDS	lamivudine	CL	a
19	2004	Mozambique	23	LIE	HIV/AIDS	stavudine	CL	a
20	2004	Mozambique	23	LIE	HIV/AIDS	nevirapine	CL	a
21	2004	Zambia	13	LMIE	HIV/AIDS	lamivudine	CL	a i
22	2004	Zambia	13	LMIE	HIV/AIDS	stavudine	CL	a i
23	2004	Zambia	13	LMIE	HIV/AIDS	nevirapine	CL	a i
24	2004	Indonesia	240	LMIE	HIV/AIDS	lamivudine	CL	a g
25	2004	Indonesia	240	LMIE	HIV/AIDS	nevirapine	CL	a g
26	2005	Ghana	24	LMIE	HIV/AIDS	all	CL	a h
27	2006	Argentina	40	UMIE	CD	oseltamivir	VL	a
28	2006	Brazil	195	UMIE	HIV/AIDS	lopinavir	Discount	a
29	2006	Thailand	69	UMIE	HIV/AIDS	efavirenz	CL	a d
30	2007	Brazil	195	UMIE	HIV/AIDS	atanazavir	Discount	a c
31	2007	Thailand	69	UMIE	HIV/AIDS	lopinavir	CL	a d
32	2007	Thailand	69	UMIE	CVD	clopidogrel	CL	a d
33	2007	Thailand	69	UMIE	NCD	letrozole	CL	a d n
34	2007	Thailand	69	UMIE	NCD	docetaxel	CL	a d n
35	2007	Thailand	69	UMIE	NCD	erlotinib	CL	a d n
36	2007	Indonesia	240	LMIE	HIV/AIDS	efavirenz	CL	f g
37	2007	Brazil	195	UMIE	HIV/AIDS	efavirenz	CL	a f
38	2007	Brazil	195	UMIE	HIV/AIDS	lopinavir	Discount	a c
39	2007	Rwanda/Canada	11	LIE	HIV/AIDS	lamivudine	CL	a f
40	2007	Thailand	69	UMIE	NCD	Imatinib	Discount	a d
41	2010	Ecuador	14	UMIE	HIV/AIDS	ritonavir	CL	a b
42	2010	Malaysia	28	UMIE	HIV/AIDS	lopinavir	NA	o
43	2012	India	1.225	LMIE	NCD	sorafenib	CL	e

Table 2.1.: List of compulsory licensing episodes

The sources for the table are: a→ Beall and Kuhn (2012a)||b→ Saez (2010)||c→ Wetzler and Ayala (2008)||d→ Wetzler and Palmedo (2008)||e→ Government of India (2012)||f→ World Health Organization (2008)||g→ Intellectual Property Watch (2007)||h→ Government of Ghana (2005)||i→ Government of Zambia (2004)||j→ Government of Malaysia (2003)||k→ World Health Organization (2010b)||l→ World Bank Group (2012)||m→ Love (2004)||n→ Baker et al. (2008)||o→ Silverman (2012). Further details are provided in appendix A.1.

In particular, information on royalty rates have been added and some episodes were updated or suppressed. Further, CL events in developed countries and renewals are not factored in, but each affected molecule is displayed in a separate row. The details on differences to Beall and Kuhn (2012b) are given in appendix A.1. The list is to be regarded as non-exclusive, because compulsory licensing is not obligatory for notification to the WTO. Only CLs for exportation under paragraph six system have to be reported and according to WTO published notifications the Rwanda & Canada case is the only one so far. (World Trade Organization (2012)).

The collection details 43 CLs or threads in 14 countries from 2000-2012 for 20 molecules marketed by 12 corporations. Figure 2.1 displays the global number of CLs issued by year, each counting one CL per molecule in a country. It gives a decent count of 25 CLs issued so far and indicates the impact of this instrument, especially taking into account voluntary licensing and discounts after a CL treat (2.2).

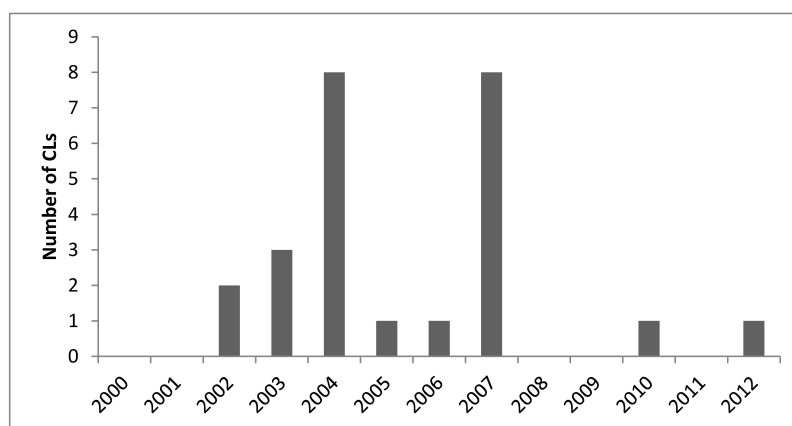


Figure 2.1.: Number of issued compulsory licenses by year

Based on Table 2.1.

In the period following the TRIPS agreement on January, 1st 1995 until 2000 no CLs were observed (Beall and Kuhn (2012b), p. 4), since fewest countries were compliant

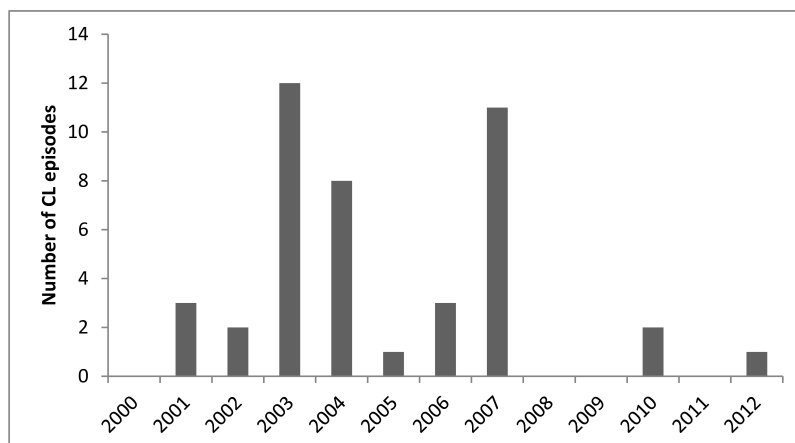


Figure 2.2.: Number of compulsory licensing episodes by year

Based on Table 2.1.

with TRIPS. The first CL activities took place just before the Doha Declaration started in 2001. 25 out of 43 episodes occurred between then and 2004, especially with regard to ARVs.

Countries that did not have the ability to produce a desired drug domestically were able to import. For example Ecuador, Malaysia, Thailand and Mozambique entrusted the drug production to Indian companies. But this happened without a CL on the Indian side, since the Indian Patent Act of 2005 only protects new patents. Also the spike in CL in 2004 after the Doha Declaration in August 2003 does not result directly from the domestic production waiver, but might rather result from the general acceptance of CL acknowledged by this conference.

Given that only Canada has undertaken a CL for export as yet, the effectiveness of paragraph 6 system is questioned. The concerns reach from the lack of "a straight forward application process" to the missing "specified formulas for calculating the level of royalties" (Chami and Wasswa-Kintu (2011)). Additionally, the time consuming process for a generic manufacturer might drive potential partners off, as can

be derived from statements by the generic manufacturer Apotex after the Canada & Rwanda case. The debate is also about complexity of the CAMR legislation process in Canada which is cumbersome.

The price of the Apotex product was not able to beat comparable Indian generics (Beall and Kuhn (2012b), page 4). The regime is under discussion since the Apotex case, but expectations of WTO are that the paragraph 6 system will be used more frequently in the future, especially with India as the exporting country (World Trade Organization (2010)). But the question is if the CL for export in the Indian legislation will prove to be automatic and encourage Indian generic manufacturers to reach out and apply for compulsory licensing.

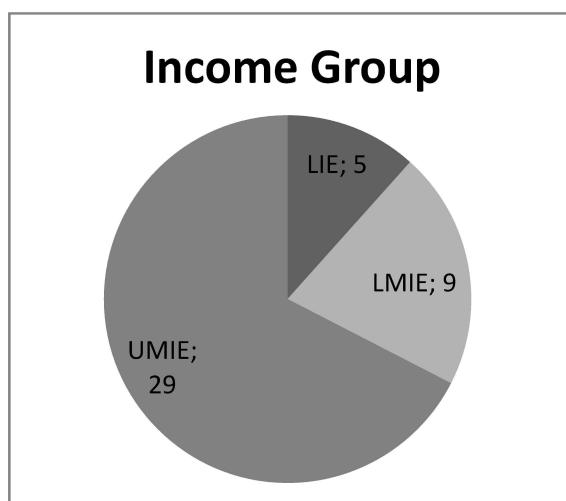


Figure 2.3.: Compulsory licensing episodes by country type based on table 2.1.

Figure 2.3 shows the split of compulsory licensing episodes by country income group. Striking is the dominance of upper-middle-income economies (UMIE) over low-income economies (LIE) and lower-middle-income economies (LMIE) by the definition of World Bank Group (2012). One explanation could be the extended transition period till 2016 granted by the WTO to least developed countries for becoming TRIPS compliant. However, Beall and Kuhn (2012b) explain that most least devel-

oped countries implemented a TRIPS compliant legislation already before 2004 and thus the unbalance is indeed due to a low propensity to issue CL in LMIE or LIE.

2.5. Debate Outline

During and after the TRIPS Agreement it has been a field of intense discussion related to medicines, besides others. Apart from the access to essential medicines the TRIPS agreement was criticized with regard to "patents on life, food security and biopiracy" (Khor and Oh (2001)). The idea of globally harmonized IPRs was especially promoted by the United States with support from most developed countries. Governments of developing countries as well as NGOs and many others opposed and heavily criticized the strictness of the agreement.

Before the Doha Ministerial Conference leading NGOs stated that the "protection of intellectual property rights is not an end in itself" (Khor and Oh (2001)). In general, the wealth transfer from developing countries to patent holders in the developed world met resistance, as Henry and Stiglitz (2010) point out. With regard to pharmaceuticals the leading critique asserts that monopolistic pricing inhibits access to drugs especially if payed out of the consumer's pocket.

Accordingly, the limitations on compulsory licensing in the TRIPS agreement were and still are a point of conflict. Developing countries and NGOs argued that due to the limitation to grant a license only to domestic manufacturers it is of no use for countries without the capacity to produce drugs. The big concern of the pharmaceutical industry lies in the fear of parallel trade to developed countries.

As depicted in section 2.3 this led to an revision of the compulsory licensing instrument and a waiver allowed for production in other countries. Additionally, a number

of countries "either agreed to opt out of using the system as importers or agreed that they would only use the system in national emergencies or extreme urgency" (Fergusson (2008) p. 16). The issuing country also has to install safeguards in order to prevent the medicines to be sold in the wrong markets. But the remuneration as well as the interpretation of the term "national emergency" is to be determined by the respective nations.

Still, the Doha round is an ongoing process of negotiations also with regard to other TRIPS related topics such as agriculture. On the topic of access to patented medicines the core discussion is on the "balance of interests between the pharmaceutical companies in developed countries that held patents on medicines and the public health needs in developing countries" (Fergusson (2008) p. 15). Yet, the required two thirds did not ratify the TRIPS amendment and thus the waiver is still in use. The paragraph 6 of the Doha declaration has only been used once and it is considered to be too cumbersome. Especially the "systems notification requirements and built-in safeguards are too costly and burdensome and represent a disincentive for the generic supplier to produce." However, detailed information on what exactly hinders least developed countries from issuing compulsory licensing and to self identify remains unanswered. Suspicions are that "attempts to use the system that were subsequently withdrawn were because of the system itself or because of other reasons such as prices" (World Trade Organization (2010)).

2.6. Conclusions and Outlook

As a first step on the way to analyze the effects of compulsory licensing this chapter gives a brief overview of global intellectual property rights and in particular the

usage of the compulsory licensing instrument. The insights from this chapter play an important role for all the following analysis. At the center of interest are the incidence and frequency of compulsory licenses as well the details of the processes involved. In order to shed light on these topics we looked into the details of several compulsory licensing episodes and present the chronology of events for South Africa, Brazil, India, Thailand, Ecuador and Rwanda. Additionally, we present an assessment of CL episodes based on research by Beall and Kuhn (2012b), validated from additional sources, completed by recent episodes and enriched with additional information.

TRIPS harmonizes patent protection across all members of the World Trade Organization (WTO). The agreement also provides a flexibility in form of the compulsory licensing (CL) instrument. By utilizing this measure a country is allowed to license a domestic pharmaceutical manufacturer with the right to produce and market a drug without approval of the right holder. This derogation is especially important for developing countries striving to improve access to essential drugs. In order to aid least developed countries lacking drug production capabilities the licenses are later cleared for export. Numerous compulsory licenses within the TRIPS environment were issued so far. Our assessment yields 43 compulsory licensing episodes, including threats to negotiate discounts. Interestingly, the evadable neglected instrument to improve drug access is frequently used, in particular with regard to drugs indicated for human immunodeficiency virus (HIV).

The detailed CL episodes illustrate a common pattern in the process of CL episodes. Each starts with a threat to issue compulsory licensing which then leads to negotiations between innovator and government. The innovator strives to protect its monopoly and usually offers a discount to prevent compulsory licensing. Simultaneously, either a government owned manufacturer is available or a private generic manufacturer applies for CL. The examples clearly highlight a trade-off which the

government faces. While CL virtually reduces health care costs a signal of endangered intellectual property protection represents costs as well, for example losses in foreign direct investment. A uniquely transparent Indian documentation of compulsory licensing negotiations between innovator, domestic generic manufacturer and government illustrates that the decision is driven by prices and implicitly the access width (Government of India (2012)). As a result of these considerations some countries issue compulsory licensing and others accept the discount.

While domestic compulsory licensing is frequently utilized the so called cross border compulsory licensing was so far applied once only. In this single case Rwanda issued CL in order to import an HIV drug from Canada, which was obliged to issue CL as well. The question remains why least developed countries without appropriate manufacturing capabilities hesitate to reach out and self identify in order to initiate the process leading to cross border compulsory licensing. As a first step in the upcoming analysis we will investigate the static duopoly that results from CL. Another important aspect is that innovator, generic manufacturer and the government of a respective country engage in negotiations prior to a potential CL. When looking at these two aspects in the context of an open economy as well as least developed countries we show that they face a structural disadvantage with regard to the negotiations. As a result CL is less beneficial.

3. Static Impact of Compulsory Licensing

Chapter 1 introduced the World Trade Organization's (WTO) agreement on "Trade Related Aspects of Intellectual Property" (TRIPS) and in particular explained that countries can use the CL instrument to introduce competition to a patented drug. Such CLs were employed frequently by developing countries, especially with regard to medications targeting HIV, so called antiretrovirals (ARVs). In order to understand the mechanics related to compulsory licensing the next step is to investigate the duopoly situation, which would result from a CL. For this purpose we ignore any dynamic effects of CL activity and assume a closed economy for now. These two additional aspects will be explored in chapters 5 and 6, respectively.

If the government of the considered developing country issues a CL the innovator (IV) faces competition from a generic competitor (GC). This duopoly situation can be modeled via price competition as prices are a basic strategic element in the pharmaceutical industry and produced quantities can easily be adjusted to the price corresponding demand (Müller-Langer (2007), p. 17). However, plain price competition and the assumption of homogeneous goods does not sufficiently reflect the situation. It is not realistic to assume that consumers only purchase the cheapest

drug and competitors sell at marginal production costs.

This chapter will start by discussing elements for developing countries that lead to imperfect competition in a duopoly. The two aspects of distribution network width and quality are motivated by papers from Chaudhuri, Goldberg, and Jia (2003), Flynn, Hollis, and Palmedo (2009) as well as Bond and Saggi (2012), which are introduced briefly. These characteristics gain a particular importance in light of neglected diseases (NDs), which predominately affect the poor population. As a next step the vertical and horizontal product differentiations are expressed formally, but not solved explicitly. In order to parameterize the effect of ND characteristics on consumer distribution, a simplified discrete model is introduced. This model covers the same differentiation and is adequate for this purpose as discussed subsequently. Most importantly the discrete duopoly model is not used to derive finding rather than to illustrate the general findings with regard to remuneration as well as negotiations in chapter 5. Finally, the remuneration for compulsory licensing is investigated and put in relation to the results.

As a result of the imperfect competition induced by distribution network width and quality, the generic competitor will not price at the marginal cost level. The distribution of profit between innovator and licensee depends on the socioeconomic prevalence of the respective disease and remuneration. The royalty rate by net sales which is used as a remuneration increases the licensee's price significantly by means of a competition as well as costs amplified effect. This royalty impact on the price based on costs as well as the result of imperfect competition are essential for understanding the discrimination of least developed countries detailed in chapter 6.

3.1. Drug Demand Characteristics in Light of Neglected Diseases

In most developing countries drugs are paid out-of-the-pocket and thus the purchase is considered by each consumer individually rather than by payers such as state or private health insurances (Chaudhuri, Goldberg, and Jia (2003), p.1). Apart from the price, other attributes play a role in this decision which lead to an imperfect duopoly competition. They drive the player's pricing decision when facing most developing countries' demand for drugs.

3.1.1. The Domestic Competitor's Distribution Network Advantage

Chaudhuri, Goldberg, and Jia (2003) shed light on the demand for drugs in developing countries by investigating the demand in India for fluoroquinolones, a sub-segment of systemic antibacterials. Using a detailed product-level data set they identify supply side parameters and expenditure elasticities by employing the so called "Almost Ideal Demand System" (Deaton and Muellbauer (1980)).¹ Chaudhuri, Goldberg, and Jia (2003) were able to allow for cross-molecule substitution by

¹The "Almost Ideal Demand System" was specified by Deaton and Muellbauer (1980) and is based on a cost function that balances between bliss $b(p)$ and mere subsistence $a(p)$ with the utility $u \in [0, 1]$. The cost function takes the form $\ln c(u, p) = (1 - u) \ln a(p) + u \ln b(p)$. Using the proposed functional forms $\ln a(p) = a_0 + \sum_k a_k \ln p_k + \frac{1}{2} \sum_k \sum_j \gamma_{kj}^* \ln p_k \ln p_j$ and $\ln b(p) = \ln a(p) + \beta_0 \prod_k p_k^{\beta_k}$ leads to the general Almost Ideal Demand System cost function:

$$\ln c(u, p) = a_0 + \sum_k a_k \ln p_k + \frac{1}{2} \sum_k \sum_j \gamma_{kj}^* \ln p_k \ln p_j + u \beta_0 \prod_k p_k^{\beta_k}. \quad (3.1)$$

The derivatives of the costs with respect to the price vector p are the quantities demanded, so that the derivative of the logarithmized costs with respect to the logarithmized price gives the budget shares w_i of good i .

grouping the products and using two levels of the demand system: While the higher level allocates the expenditures between molecules, the lower level is designed to estimate parameters within a fluoroquinolones molecule for different manufacturers. While allowing for expenditure switches at the higher level of the system, Chaudhuri, Goldberg, and Jia (2003) investigate the welfare losses in counterfeit scenarios with the estimates in hand. By withdrawing one or more domestic competitors from the system the compensation variation is applied as a measure for welfare losses.

Product Group	Elasticity with Respect to:							
	Prices of Foreign Product Groups			Prices of Domestic Product Groups				Overall Quinolones Expenditure
	Cipro	Norflo	Oflo	Cipro	Norflo	Oflo	Sparflo	
Foreign Ciprofloxacin	-5.57* (1.79)	-0.13 [†] (0.07)	-0.15* (0.07)	4.01* (1.84)	0.11 [†] (0.06)	0.11 [†] (0.06)	0.16* (0.06)	1.37* (0.29)
Foreign Norfloxacin	-4.27 [†] (2.42)	-0.45 (1.12)	-4.27 [†] (2.42)	3.50 [†] (2.10)	-6.02 (6.23)	4.51* (1.84)	4.65* (1.83)	2.20* (1.05)
Foreign Ofloxacin	-0.11* (0.05)	-0.10 [†] (0.05)	-1.38* (0.31)	-0.09 (0.27)	0.09 [†] (0.05)	0.23 (0.28)	0.11* (0.04)	1.16* (0.17)
Domestic Ciprofloxacin	0.18* (0.08)	0.01* (0.00)	-0.01 (0.01)	-1.68* (0.23)	0.08* (0.02)	0.08* (0.02)	0.10* (0.02)	1.17* (0.03)
Domestic Norfloxacin	0.04* (0.01)	-0.03 (0.03)	0.04* (0.01)	0.58* (0.17)	-2.23* (0.11)	0.42* (0.04)	0.40* (0.03)	0.73* (0.09)
Domestic Ofloxacin	0.05* (0.02)	0.05* (0.02)	0.11 (0.13)	0.77* (0.28)	0.74* (0.08)	-3.42* (0.25)	0.74* (0.08)	0.89* (0.21)
Domestic Sparfloxacin	0.07* (0.02)	0.04* (0.01)	0.07* (0.02)	1.15* (0.15)	0.63* (0.06)	0.63* (0.06)	-2.88* (0.17)	0.28* (0.12)

Notes: Standard errors in parentheses. Elasticities evaluated at average revenue shares. Asterisk (*) denotes significance at the 5% significance level, and stagger (†) denotes significance at the 10% level.

Table 3.1.: Estimated cross-price elasticities by Chaudhuri, Goldberg, and Jia (2003) (table 6a): While the diagonal values are (negative) own price elasticities, the last column displays the elasticities of overall expenditure in the segment. The remaining values are estimated cross-price elasticities, which are striking large and positive between different domestic product groups.

A major finding is that domestic manufacturers face a relatively high rate of substitution when competing with each other, compared to competing with a multinational company. Table 3.1 shows these estimated cross price elasticities in the bottom right quarter. Also, the welfare loss from withdrawing domestic manufacturers exceeds the

loss induced by a price increase. The reason for their finding appears to be the wider retail range of domestic manufacturers due to a more extensive network of pharmacies that stock their products. The "domestic products are more readily available to Indian consumers than products produced by foreign subsidiaries" as Chaudhuri, Goldberg, and Jia (2003) (p. 4) explain. A multinational innovator usually does not cover the entire country, especially not the rural areas. This is also plausible considering that generic manufacturers typically offer a much larger portfolio than innovators.

If a compulsory licensing is issued a multinational innovator will face competition from a domestic generic distributor. Given the findings of Chaudhuri, Goldberg, and Jia (2003) a geographic horizontal distinction between these competitors can not be neglected when analyzing the impact of compulsory licensing (CL). This holds especially since a government could enhance consumer welfare by licensing a domestic generic competitor with a comprehensive distribution network.

3.1.2. The Innovator's Quality Advantage

Quality concerns are not relevant for consumers in many developed nations, since regulators and payers address this problem. In developing countries, however, out-of-the pocket payment leads to a higher relevance of consumer preferences, weighting quality and costs. A number of studies investigate the duopoly for a drug with respect to the entry of generic competition due to patent expiry and emphasize the importance of perceived quality differentiation (Regan (2007), Cabrales (2003)). Not only can a quality difference be perceived by consumers, but might as well be reasonable regarding the production of generics in developing countries. Thailand and Brazil give striking examples of quality concerns after issuing CLs as described

in section 2.2: While the licensed Brazil manufacturer FarManguinhos lagged the technological knowledge to produce the drug for two years, the Thailand Government Pharmaceutical Organization (GPO) is not able to deliver the desired quality to date. For both countries Indian manufacturers supplied the drugs but even they might face quality problems. For example, the European Medicines Agency has recommended the recall of a generic clopidogrel from the Swiss manufacturer Acino in 2010 produced in an Indian factory. This recommendation was motivated by a failure of good manufacturing practice in an Indian plant (Hirschler (2010) - *EU plans recall of Indian-made generic Plavix*).

Such (perceived) quality differences can be projected to consumer preferences via vertical differentiation. For example Bond and Saggi (2012) use a simple model of vertical differentiation for compulsory licensing, arguing in a similar way. For Bond and Saggi (2012) the duopoly resulting from CL is part of a game in which they investigate the behavior of a "southern" government and a "northern" innovator with regard to CL. The employed model assumes a utility of $U = \Delta q - p$ per consumer, whereas p denotes the product price and q is the products quality. The consumers differ in their willingness to pay Δ for quality and are uniformly distributed over $\Delta \in [0, 1]$. However, this assumption of uniform distributed consumers might not be adequate as Flynn, Hollis, and Palmedo (2009) point out, especially when investigating CL in developing countries. Indeed, the following will show how consumer welfare and company profits change dramatically and thus make a difference on decisions.

3.1.3. Income Inequality and Neglected Diseases

When drugs are payed out-of the pocket the most important restriction on consumer preferences is the budget they can spend. Flynn, Hollis, and Palmedo (2009) elabo-

rate this matter and argue that convexity of demand is induced by income inequality in developing countries since patients in need of essential medicines are most likely to spend whatever they have available. Convex demand implies that while the lower income segment of the market is highly price elastic the other is not. Monopolists are then tempted to serve only a smaller (high income) segment of the market, price their drug high while maximizing profits, but causing a large deadweight loss on the consumer side. Clearly, for essential medicines deadweight losses describe no other but the denial of access to essential treatment. Flynn, Hollis, and Palmedo (2009) bring this forward to justify compulsory licensing in developing countries generally.

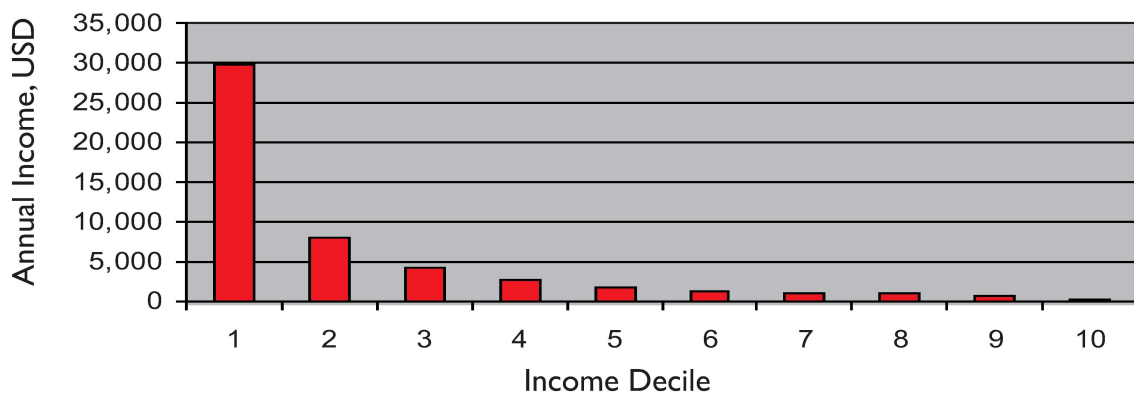


Figure 3.1.: South Africa Distribution of Income from Flynn, Hollis, and Palmedo (2009), figure 3. The graph shows the distribution of average per capita income for population deciles in South Africa in 2000.

The authors substantiate the argument by means of income distribution in developing countries, as an example in figure 3.1 for South Africa. By assuming that the ability to pay is proportional to income and uniform incidence across income levels Flynn, Hollis, and Palmedo (2009) derive the demand in figure 3.2. This demand curve is highly convex and emphasizes that companies will exclude a large low income segment while pricing high. Figure 3.3 shows the respective revenue gained by a monopolist when pricing according to the demand function per quantity. The

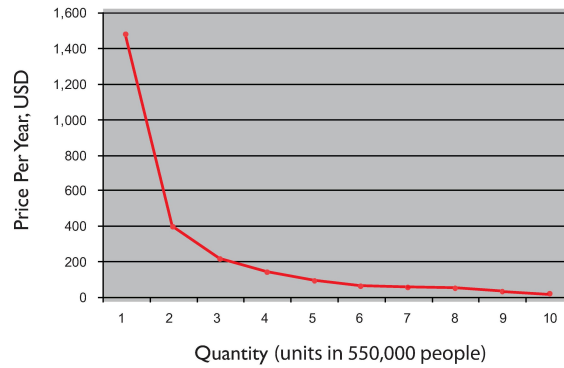


Figure 3.2.: Exemplary South Africa demand curve from Flynn, Hollis, and Palmedo (2009), figure 4.1. The Figure gives the estimated demand assuming that the ability to pay is proportional (5%) to the income in figure 3.1 and incidence equal across income levels.

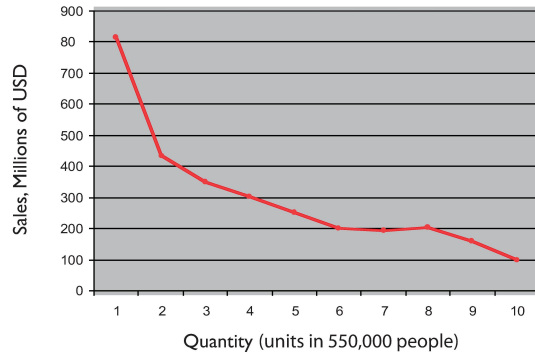


Figure 3.3.: Exemplary South Africa sales revenue from Flynn, Hollis, and Palmedo (2009), figure 4.2. It shows companies revenue while satisfying the price conditions required to sell the respective quantities.

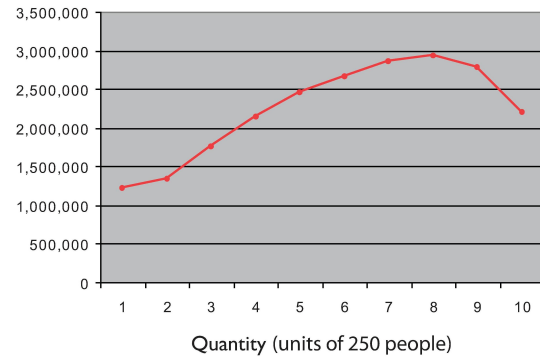


Figure 3.4.: Exemplary Norway sales revenue from Flynn, Hollis, and Palmedo (2009), figure 5.2. Similar to figure 3.3.

optimal monopolistic price would only serve the first income decile. The importance of income becomes evident when comparing this with Norway, derived in the same way and shown in figure 3.4.

The assumption of uniform incidence across income levels serves the purpose of demonstrating the income distribution effect on monopolistic pricing behavior. However, it is not adequate when it comes to compulsory licensing for neglected diseases (ND) predominantly affecting the poor population in developing countries.

3.2. Asymmetric Duopoly Model

The following will explain an idealized two dimensional demand model which accounts for the two factors of vertical and horizontal differentiation discussed above. While this model is not used going forward, a more practical model of asymmetric demand is introduced which permits to actuate ND characteristics. This model is used to illustrate other findings with regard to remuneration or negotiations

3.2.0.1. Two Dimensional Demand

The upcoming utilizes a generalization of Hotelling's location model with 2 characteristics, which are quality and location as argued above (Hotelling (1929)).² Only price competition is relevant here because characteristics are assumed to be already formed. All parameters concerning this model are tagged with a tilde (as in \tilde{x}) to avoid confusion with other models.

The innovator (IV) and generic competitor (GC) compete in the characteristics of location and quality which are described by the vector $\tilde{i} = \{\tilde{i}_Q, \tilde{i}_L \in [0, 1]\}$ for a company \tilde{i} , that is $\tilde{v} = \{\tilde{v}_Q, \tilde{v}_L \in [0, 1]\}$ and $\tilde{g}c = \{\tilde{g}c_Q, \tilde{g}c_L \in [0, 1]\}$. Each consumer type \tilde{c} is characterized in the same area by $\tilde{c} = \{\tilde{c}_Q, \tilde{c}_L \in [0, 1]\}$ and they are distributed by $\tilde{f}\{\tilde{c}_Q, \tilde{c}_L\}$ over the respective area $\tilde{C} = [0, 1]^2$.

An important effect of compulsory licensing is the improved access to drugs, which

²Apart from Hotelling (1929), two frequently cited works in this are are Caplin and Nalebuff (1991) and Irmen and Thisse (1996). Whereas Caplin and Nalebuff (1991) provide a prove on the existence of a price equilibrium, Irmen and Thisse (1996) employ a sequential game in which firms first form the characteristics and then compete in prices to reveal that in their setting minimum differentiation occurs in all but one characteristic. Caplin and Nalebuff (1991) approach is more general and they show that for n characteristics and i products and given linearity of consumers preferences in characteristics as well as a ρ -concave consumer's distribution across these characteristics, a price equilibrium exists. Additionally, for $i=2$ this equilibrium is unique.

can be captured by incorporating a budget restriction. Let \tilde{c}_I be the income of a respective consumer with $\tilde{c}_I \in [0, 1]$. \tilde{c}_I can be assumed to be linked to \tilde{c}_Q directly, in particular $\tilde{c}_I = \tilde{c}_Q$. In developing countries consumers can not lend money for medications easily so that the budget restriction $\tilde{c}_I = \tilde{c}_Q > p$ must hold for any price \tilde{p} of the drug that is purchased.

The utilities of a consumer purchasing the medication from *IV* or *GC* are given by

$$\begin{aligned}\tilde{U}_{IV}(\tilde{c}) &= \tilde{S} + \tilde{v}_Q \cdot \tilde{c}_Q + \tilde{v}_l \cdot \tilde{c}_l + \tilde{c}_Y - \tilde{p}_{IV} \text{ and} \\ \tilde{U}_{GC}(\tilde{c}) &= \tilde{S} + \tilde{g}_Q \cdot \tilde{c}_Q + \tilde{v}_l \cdot \tilde{c}_l + \tilde{c}_Y - \tilde{p}_{GC}.\end{aligned}$$

The constant \tilde{S} denotes the gross consumer surplus of using any of the two drugs and equals across all consumer types. Quality characteristics are preset and maximum as well as minimum (perceived) quality is represented by the two competitors so that $\tilde{v}_Q = 1$ and $\tilde{g}_Q = 0$. *GC* is assumed to have a very broad distribution network available and consumers in rural area can access the drug optimally compared to *IV* so that $\tilde{v}_l = 0$ and $\tilde{g}_l = 1$. Consumers located in the rural area value a distribution network most and are characterized by $\tilde{c}_l = 1$.

A consumer will decide to use *GC*'s drug, if $\tilde{U}_{GC}(\tilde{C}) \geq \tilde{U}_{IV}(\tilde{C})$ and thus the consumer's indifference curve is defined by $\tilde{U}_{GC}(\tilde{C}) = \tilde{U}_{IV}(\tilde{C})$. The indifferent consumer satisfies

$$\begin{aligned}\tilde{U}_{IV}(c) &= \tilde{U}_{GC}(c) \\ \tilde{S} + \tilde{v}_Q \cdot \tilde{c}_Q + \tilde{v}_L \cdot \tilde{c}_L + \tilde{c}_Y - \tilde{p}_{IV} &= \tilde{S} + \tilde{g}_Q \cdot \tilde{c}_Q + \tilde{v}_L \cdot \tilde{c}_L + \tilde{c}_Y - \tilde{p}_{GC} \\ \tilde{S} + 1 \cdot \tilde{c}_Q + 0 \cdot \tilde{c}_L + \tilde{c}_Q - \tilde{p}_{IV} &= \tilde{S} + 0 \cdot \tilde{c}_Q + 1 \cdot \tilde{c}_L + \tilde{c}_Q - \tilde{p}_{GC} \\ \tilde{c}_Q - \tilde{p}_{IV} &= \tilde{c}_L - \tilde{p}_{GC}\end{aligned}$$

and a consumer prefers IV 's product for $\tilde{c}_Q \geq \tilde{p}_{IV} + \tilde{c}_L - \tilde{p}_{GC}$. If additionally $\tilde{c}_Q \geq \tilde{p}_{IV}$ the consumer can afford it and accordingly the demand is given by

$$\begin{aligned}\tilde{D}_{IV} &= \iint_{\tilde{C}_{IV}} \tilde{f}(\tilde{c}_Q, \tilde{c}_L) d\tilde{c}_Q d\tilde{c}_L \text{ and} \\ \tilde{D}_{GC} &= \iint_{\tilde{C}_{GC}} \tilde{f}(\tilde{c}_Q, \tilde{c}_L) d\tilde{c}_Q d\tilde{c}_L,\end{aligned}$$

whereas

$$\begin{aligned}\tilde{C}_{IV} &= \{\tilde{c}_Q, \tilde{c}_L \in [0, 1]^2 \mid \tilde{c}_Q \geq \tilde{p}_{IV} \text{ and } \tilde{c}_Q \geq \tilde{p}_{IV} + \tilde{c}_L - \tilde{p}_{GC}\} \\ \tilde{C}_{GC} &= \{\tilde{c}_Q, \tilde{c}_L \in [0, 1]^2 \mid \tilde{c}_Q \geq \tilde{p}_{GC} \text{ and } \tilde{c}_Q < \tilde{p}_{IV} + \tilde{c}_L - \tilde{p}_{GC}\}.\end{aligned}$$

This duopoly model gives the vertical and horizontal differentiation in a continuous way. However, the budget restrictions do not satisfy the condition of linear consumer's preferences which are sufficient for a price equilibrium as depicted by Caplin and Nalebuff (1991). A price equilibrium is numerically computable over the relevant area, but not practically with a parameter α measuring neglected disease (ND) characteristics in the consumer's demand. This parameter α would control the non-uniform consumer distribution by allocating more consumers with strong budget restrictions in the rural area for NDs.

Yet, it is important to compare the impact of CL on a drug designed to treat ND to a CL on medications for global diseases. For NDs, per definition the patients are more likely to be located in rural areas than in developed cities and ND affect predominantly the poor. This will effect both, vertical as well as horizontal differentiation,

by means of budget and location changes in the consumer distribution. In order to understand the impact of CL induced competition for ND the following will derive a simpler model which additionally fits the reality better, as will be described in the next chapter 5.

3.2.0.2. Discrete Asymmetric Duopoly Model

In order to address the above effects a plausible approach is to utilize a non-continuous consumer distribution and to consider two distinct consumer types $\hat{\Theta}$. All parameters concerning the discrete asymmetric duopoly model are tagged with a hat (as in \hat{x}) to avoid confusion with other models. An innovator (IV) which sells a medication in developing countries might exclude a portion $\hat{\alpha}$ of patients from treatment, depending on the drug price as well as the distribution network. Generally, for NDs more patients ($\hat{\alpha}$) would be affected by these attributes than for global diseases as section 3.1.3 describes. For simplicity, both attributes are factored into the same parameter, assuming that poverty comes along with rural settlement or vice versa. These $\hat{\alpha}$ consumers $\hat{\Theta}$, which are not reached by IV in a monopoly situation, are for notation and simplicity reasons described as located in the rural area (\hat{RA}). Accordingly, they are of the type $\hat{\Theta}_{\hat{RA}}$ contrary to consumers in the city $\hat{\Theta}_{\hat{CY}}$.

While per definition IV does not have access to the $\hat{\alpha}$ patients of type $\hat{\Theta}_{\hat{RA}}$, or vice versa, a domestic generic competitor GC could sell the drug to these consumers. This is assumed to hold absolutely for matters of distribution network by means of Chaudhuri, Goldberg, and Jia (2003), while consumer's budget distribution as well as GC 's price determine access in terms of budget. The revenue of GC in rural areas $\hat{\Pi}_{GC}^{\hat{RA}}(\hat{\alpha}, \hat{p}_{GC})$ is given by $\hat{D}_{GC}^{\hat{RA}}(\hat{p}_{GC})\hat{p}_{GC}$, with the demand $\hat{D}_{GC}^{\hat{RA}}(\hat{p}_{GC})$ decreasing in \hat{p}_{GC} .

Both firms IV and GC have access to the consumers of type $\hat{\Theta}_{C\hat{T}Y}$, who choose between the two drugs IV and GC that compete in a setting of vertical differentiation without budget constraints. $\hat{\Theta}_{C\hat{T}Y}$ can afford any drug and chooses between the two products in consideration of price and quality.

Let the distribution of consumers $\hat{\Theta}_{C\hat{T}Y}$ be uniform and normalized to $\int_0^1 \hat{f}(\hat{c}_Q) d\hat{c}_Q = 1$. The consumer's preferences are linearly determined by the valuation of quality $\hat{c}_Q \in [0, 1]$, the utility \hat{S} of consuming any drug and the prices \hat{p}_{IV} and \hat{p}_{GC} . The drugs IV and GC are differentiated via the qualities $\hat{v}_Q = 1$ and $\hat{g}_Q = 0$ so that the preferences for each drug are give by

$$\begin{aligned}\hat{U}_{\hat{c}}^{IV}(\hat{p}_{IV}, \hat{p}_{GC}, \hat{c}_Q) &= \hat{S} + \hat{c}_Q \cdot \hat{v}_Q - \hat{p}_{IV} \\ &= \hat{S} + \hat{c}_Q - \hat{p}_{IV} \text{ and} \\ \hat{U}_{\hat{c}}^{GC}(\hat{p}_{IV}, \hat{p}_{GC}, \hat{c}_Q) &= \hat{S} + \hat{c}_Q \cdot \hat{g}_Q - \hat{p}_{GC} \\ &= \hat{S} - \hat{p}_{GC}.\end{aligned}$$

A consumer with $\hat{c}_Q = \hat{p}_{IV} - \hat{p}_{GC}$ thus is indifferent between consuming IV or GC . Accordingly,

$$\begin{aligned}\hat{D}_{GC}^{C\hat{T}Y}(\hat{p}_{IV}, \hat{p}_{GC}) &= \int_0^{\hat{p}_{IV} - \hat{p}_{GC}} \hat{f}(\hat{c}_Q) d\hat{c}_Q \\ \Leftrightarrow \hat{D}_{GC}^{C\hat{T}Y}(\hat{p}_{IV}, \hat{p}_{GC}) &= \hat{p}_{IV} - \hat{p}_{GC}\end{aligned}\tag{3.2}$$

and

$$\begin{aligned}\hat{D}_{IV}^{C\hat{T}Y}(\hat{p}_{IV}, \hat{p}_{GC}) &= \int_{\hat{p}_{IV} - \hat{p}_{GC}}^1 \hat{f}(\hat{c}_Q) d\hat{c}_Q \\ \Leftrightarrow \hat{D}_{IV}^{C\hat{T}Y}(\hat{p}_{IV}, \hat{p}_{GC}) &= 1 + \hat{p}_{GC} - \hat{p}_{IV}\end{aligned}\tag{3.3}$$

$$= 1 - \hat{D}_{GC}^{CTY}(\hat{p}_{IV}, \hat{p}_{GC})$$

give the demand for both products in the city.

While the total profit for GC depends on \hat{D}_{GC}^{CTY} as well as $\hat{D}_{GC}^{\hat{R}A}$, the innovator IV only sells \hat{D}_{IV}^{CTY} in the city. Ignoring, for now, any remunerations paid from GC to IV the profits are given by

$$\hat{\Pi}_{GC} = (1 - \hat{\alpha})\hat{p}_{GC}\hat{D}_{GC}^{CTY} + \hat{\alpha}\hat{p}_{GC}\hat{D}_{GC}^{\hat{R}A} \text{ and} \quad (3.4)$$

$$\hat{\Pi}_{IV} = (1 - \hat{\alpha})\hat{p}_{IV}\hat{D}_{IV}^{CTY}. \quad (3.5)$$

The parameter $\hat{\alpha} \in [0, 1]$ controls the ND characteristics in the consumer's demand. For example, while a drug targeting diabetes type 2 ($\hat{\alpha} = 0$) might face full competition, a medication treating dengue fever ($\hat{\alpha} = 1$) will predominantly affect the poor in rural areas.

The optimal price \hat{p}_{IV}^* is determined by optimizing 3.4 with the demand in 3.3. Without specifying the demand in rural areas $\hat{D}_{GC}^{\hat{R}A}$, this leads to

$$\max_{\hat{p}_{IV}} \hat{\Pi}_{IV} = (1 - \hat{\alpha})(1 + \hat{p}_{GC} - \hat{p}_{IV})\hat{p}_{IV} \quad (3.6)$$

$$\Rightarrow 0 = (1 - \hat{\alpha})(1 + \hat{p}_{GC} - 2\hat{p}_{IV}^*) \quad (3.7)$$

$$\Rightarrow \hat{p}_{IV}^*(\hat{p}_{GC}) = \frac{1 + \hat{p}_{GC}}{2} \quad (3.8)$$

as a reaction to \hat{p}_{GC} with $\frac{\partial^2 \hat{\Pi}_{IV}}{\partial \hat{p}_{IV}^2} = 2\hat{\alpha} - 2 \leq 0$ since $\hat{\alpha} \leq 1$.

The implications of vertical and horizontal differentiation in this setup on IV 's profits are demonstrated in picture 3.5. It gives the profit of IV for a given price \hat{p}_{GC} with the optimal reaction \hat{p}_{IV} by IV in the absence of any remuneration. While

a Bertrand price competition would result in zero profits, the quality advantage of *IV* accounts for a positive profit of *IV* even though competition occurs. For sole quality competition the optimal equilibrium price of *GC* would be $\hat{p}_{GC} = \frac{1}{3}$ and the red line in picture 3.5 indicates the resulting profits of *IV* for a given $\hat{\alpha}$ with $\hat{p}_{IV}^* = \frac{1+\hat{p}_{GC}}{2} = \frac{2}{3}$. However, plain vertical differentiation such as employed by Bond and Saggi (2012) is not sufficient in a CL scenario when considering NDs. For diseases predominately affecting the poor, quality becomes less important while consumer budgets and distribution give domestic generic manufacturer an advantage.

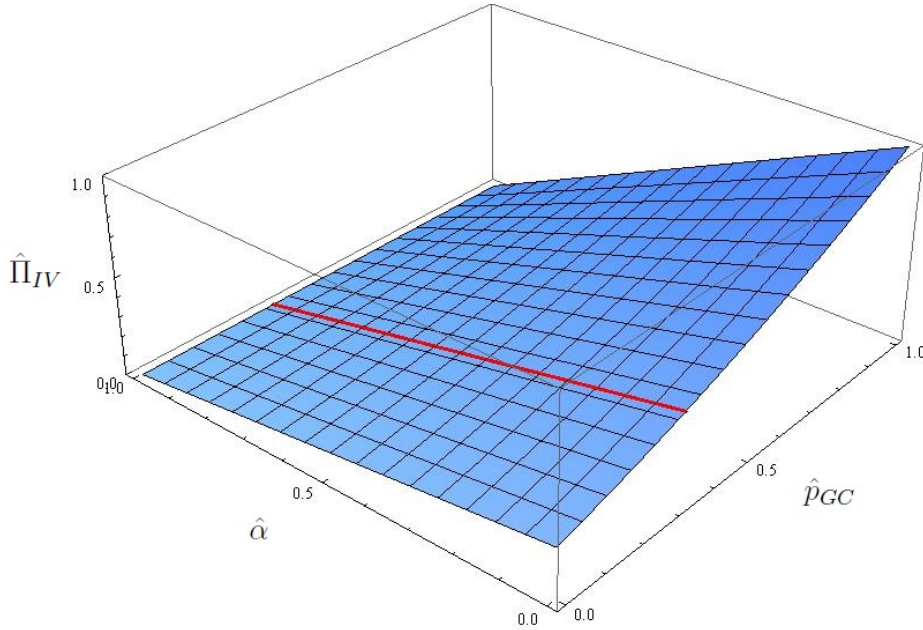


Figure 3.5.: The Innovator's profit in dependence of price \hat{p}_{GC} and neglected disease characteristics α , while ignoring any remuneration. The red line indicates the profit in case of pure vertical differentiation ($\hat{p}_{GC} = \frac{1}{3}$).

With regard to the optimization ratio of *GC* it would be problematic to assume any demand function for the rural area. In fact, considering \hat{p}_{GC} as a given parameter is sufficient for the results since it is subject to negotiations rather than demand as chapter 5 will clarify.

3.3. Remuneration and Compulsory Licensing

Rarely discussed in economic literature related to compulsory licensing are the terms of remuneration, which a potential patentee is obligated to pay the innovator. Structure and height of this transfer are not settled by the WTO TRIPS agreement, but chosen by the respective government. In practice a small royalty per sales applies and table 3.2 gives the actual compulsory licenses chronologically based on table 2.1. It includes information on the involved parties as well as the respective royalty rates. For Zimbabwe, Egypt and Ghana the royalty rates are not available.

Row	Episode Period	Nation	Molecule	IV	Distributor	Royalty	Sources
1	2002	Zimbabwe	all	ALL	Varichem Pharmaceuticals Ltd	NA	a
2	2002	Egypt	sildenafil	PFIZER	all	NA	a
3	2003	Malaysia	lamivudine	GSK	Syarikat Megah Pharma	waived by IV	a j m
4	2003	Malaysia	didanosine	BMS	Syarikat Megah Pharma	waived by IV	a j m
5	2003	Malaysia	zidovudine	GSK	Syarikat Megah Pharma	waived by IV	a j m
6	2004	Mozambique	lamivudine	GSK	Pharco Moçambique Lda	20,0%	a
7	2004	Mozambique	stavudine	BMS	Pharco Moçambique Lda	20,0%	a
8	2004	Mozambique	nevirapine	BI	Pharco Moçambique Lda	20,0%	a
9	2004	Zambia	lamivudine	GSK	Pharco Ltd.	2,5%	a i
10	2004	Zambia	stavudine	BMS	Pharco Ltd.	2,5%	a i
11	2004	Zambia	nevirapine	BI	Pharco Ltd.	2,5%	a i
12	2004	Indonesia	lamivudine	GSK	PT Kimia Farma	0,5%	a g
13	2004	Indonesia	nevirapine	BI	PT Kimia Farma	0,5%	a g
14	2005	Ghana	all	ALL	Government	NA	a h
15	2006	Thailand	efavirenz	MERCK	GPO	0,5%	a d
16	2007	Thailand	lopinavir	ABBOTT	GPO	0,5%	a d
17	2007	Thailand	clopidogrel	SANOFI-AVENTIS	GPO	0,5%	a d
18	2007	Thailand	letrozole	NOVARTIS	GPO	3%-5%	a d n
19	2007	Thailand	docetaxel	SANOFI-AVENTIS	GPO	3%-5%	a d n
20	2007	Thailand	erlotinib	ROCHE	GPO	3%-5%	a d n
21	2007	Indonesia	efavirenz	MERCK	PT Kimia Farma	0,5%	f g
22	2007	Brazil	efavirenz	MERCK	FarManguinhos	1,5%	a f
23	2007	Rwanda/Canada	lamivudine	GSK	Camerwa	2,0%	a f
24	2010	Ecuador	ritonavir	ABBOTT	Eskegroup SA	TRM	a b
25	2012	India	sorafenib	BAYER	Natco Pharma	6,0%	e

Table 3.2.: Compulsory licenses and remunerations. Sources, definitions on acronyms for companies and other details are provided in appendix A.1.

It is striking that all remunerations are royalties, rather than a lump sum. Further,

all but one country applied a royalty based on the net sale of GC . Only Ecuador used the so called "Tiered Royalty Method" (TRM) which is based on prices in the developed world rather than the net sales. This approach is detailed further below. Most significantly, the royalty rates are quite low, ranging between 0.5% and 6% with Mozambique being the only exception.

3.3.1. General Royalty Effects on the Licensee's Price

Economic considerations on the remuneration are set out by Tirole (2006): Proportional royalties based on the sales, and thus acting as a tax, would better "reflect the size of the market for a particular pharmaceutical (for example, how widespread the disease is in the country)" (Tirole (2006), p. 315). On the contrary, a single payment could better differentiate between low income and middle income countries. The WHO recommends a tiered royalty method suggested by Love (2005), which is based on the patented drug price in high income countries rather than the generic drug price in the considered developing country (Love (2005) pp. 7). The recommendation fixes the royalty at 4% but is adjusted by the relative income per capita. This tiered royalty method was applied by Ecuador compulsory licensing for ritonavir, which is depicted in section 2.2. Both, Tirole (2006) and Love (2005) acknowledged that a royalty by sales increases the price of the respective generic drug and accordingly reduces access in the absence of any covering health insurance.

Generally, the profit of GC when paying a royalty based on net sales is given by

$$\Pi_{GC} = D_{GC}(p_{GC}, p_{IV})((1 - r)p_{GC} - vc) \quad (3.9)$$

with variable costs vc and royalty r per sales. If the second order conditions are

satisfied, the optimal price for GC is given by

$$\begin{aligned} p_{GC}^* &= \frac{D_{GC}(p_{GC}, p_{IV})}{-\frac{\partial D_{GC}(p_{GC}, p_{IV})}{\partial p_{GC}}} + \frac{vc}{1-r}, \text{ or} \\ \Leftrightarrow p_{GC}^* &= \frac{D_{GC}(p_{GC}, p_{IV})}{-\frac{\partial D_{GC}(p_{GC}, p_{IV})}{\partial p_{GC}}} + vc + vc \frac{r}{1-r}. \end{aligned} \quad (3.10)$$

The direct royalty effect $vc \frac{r}{1-r}$ on the optimal price p_{GC}^* depends on the production costs vc . This costs amplified royalty effect is in line with Tirole (2006), who states that a royalty "would not affect the final price much, especially for those medicines with low production costs". However, competition further amplifies the royalty effect on p_{GC}^* , since the optimal price of IV changes in r as well. Intuitively, with the introduction of a royalty by sales IV has an interest in GC 's demand. The profit of IV with royalty is given by

$$\Pi_{IV} = D_{IV}(p_{IV}, p_{GC})(p_{IV} - vc) + r p_{GC} D_{GC}(p_{GC}, p_{IV}), \quad (3.11)$$

assuming that IV and GC face equivalent production costs vc per unit. If the second order conditions are satisfied, the optimal price for IV is

$$p_{IV}^* = \frac{D_{IV}(p_{IV}, p_{GC})}{-\frac{\partial D_{IV}(p_{IV}, p_{GC})}{\partial p_{IV}}} + vc + r \cdot p_{GC} \frac{\partial D_{GC}(p_{GC}, p_{IV})}{\partial p_{IV}}. \quad (3.12)$$

The difference to an optimal price for IV in the absence of royalty payments lies in $r \cdot p_{GC} \frac{\partial D_{GC}(p_{GC}, p_{IV})}{\partial p_{IV}}$, which is positive for $r > 0$ under the assumption of $\frac{\partial D_{GC}(p_{GC}, p_{IV})}{\partial p_{IV}} \geq 0$. The effect of p_{IV} on $D_{GC}(p_{GC}, p_{IV})$ depends on the intensity of competition but it is intuitive to assume this effect to be non-negative, so that $\frac{\partial D_{GC}(p_{GC}, p_{IV})}{\partial p_{IV}} > 0$ holds. The next question is how GC reacts to this increased price. The derivative of 3.10

with regard to p_{IV} leads to

$$\frac{\partial p_{GC}^*}{\partial p_{IC}} = \frac{\frac{\partial D_{GC}(p_{GC}, p_{IV})}{\partial p_{IV}} \cdot \left(-\frac{\partial D_{GC}(p_{GC}, p_{IV})}{\partial p_{GC}}\right) - D_{GC}(p_{GC}, p_{IV}) \cdot \left(-\frac{\partial^2 D_{GC}(p_{GC}, p_{IV})}{\partial p_{GC} \partial p_{IV}}\right)}{\left(-\frac{\partial D_{GC}(p_{GC}, p_{IV})}{\partial p_{GC}}\right)^2}.$$

This expression is positive for:

$$\frac{\partial D_{GC}(p_{GC}, p_{IV})}{\partial p_{IV}} \geq 0, \quad (3.13)$$

$$\frac{\partial D_{GC}(p_{GC}, p_{IV})}{\partial p_{GC}} \leq 0 \text{ and} \quad (3.14)$$

$$-\frac{\partial^2 D_{GC}(p_{GC}, p_{IV})}{\partial p_{GC} \partial p_{IV}} \leq 0. \quad (3.15)$$

While the assumption 3.13 is reasonable and already used for 3.12, assumption 3.14 is straight forward as well. Assumption 3.15 might not be clear at first sight but matches intuition when phrasing it. It demands that the "negative effect of increasing p_{GC} on GC 's demand decreases in the innovator's price p_{IV} ". This is not necessary but simplifies the interpretation: For higher p_{IV} , the consumers are less price sensitive with regard to p_{GC} . In fact, it would be necessary that an actual positive effect of increasing p_{IV} on $\frac{\partial D_{GC}(p_{GC}, p_{IV})}{\partial p_{GC}}$ is not too high.

The argumentation here follows intuition: With the introduction of a royalty, IV is interested in GC 's profit and a higher price p_{IV} now additionally increases the royalty profit apart from the income per unit. This consideration increases the optimal price and the desired effect occurs: GC 's demand increases and GC in turn adjusts by increasing the price p_{GC} . Summarizing, a royalty by sales does increase the price of the generic drug to a greater extend than anticipated. Any competition, which innovator and generic manufacturer certainly engage in, increase the royalty's effect on the price additionally to the cost amplified royalty effect. This only holds for royalties based on net sales and not for the tiered royalty method.

In order to demonstrate the impact of a royalty on price and access the following will apply this general concept to the discrete asymmetric duopoly model.

3.3.2. Exemplary Demonstration of Royalty Effects

Introducing a net sales based royalty and variable costs in the discrete asymmetric demand model changes the profit functions of GC (3.4) and IV (3.5) to

$$\bar{\Pi}_{IV} = (1 - \bar{\alpha})\bar{D}_{IV}^{CTY}(\bar{p}_{IV} - vc) + (1 - \bar{\alpha})r\bar{p}_{GC}\bar{D}_{GC}^{CTY} + \bar{\alpha}r\bar{p}_{GC}\bar{D}_{GC}^{\bar{R}A} \text{ and} \quad (3.16)$$

$$\bar{\Pi}_{GC} = (1 - \bar{\alpha})\bar{D}_{GC}^{CTY}((1 - r)\bar{p}_{GC} - vc) + \bar{\alpha}\bar{D}_{GC}^{\bar{R}A}((1 - r)\bar{p}_{GC} - vc). \quad (3.17)$$

Assuming full competition with $\bar{\alpha} = 0$ enables us to investigate the above depicted effects. Then, $\bar{\alpha}\bar{D}_{GC}^{\bar{R}A} = 0$ and thus IV and GC engaging in plain vertical differentiation with a royalty r , so that

$$\bar{\Pi}_{IV}^{\bar{\alpha}=1} = \bar{D}_{IV}^{CTY}(\bar{p}_{IV} - vc) + r\bar{p}_{GC}\bar{D}_{GC}^{CTY} \text{ and}$$

$$\bar{\Pi}_{GC}^{\bar{\alpha}=1} = \bar{D}_{GC}^{CTY}((1 - r)\bar{p}_{GC} - vc).$$

The demand functions \bar{D}_{IV}^{CTY} and \bar{D}_{GC}^{CTY} stay untouched and from the demand functions 3.2 and 3.3 we get the objective profit functions

$$\begin{aligned} \max_{\bar{p}_{IV}} \bar{\Pi}_{IV}^{\bar{\alpha}=1} &= (\bar{p}_{IV} - vc)(1 + \bar{p}_{GC} - \bar{p}_{IV}) + r\bar{p}_{GC}(\bar{p}_{IV} - \bar{p}_{GC}) \\ &\Rightarrow 0 = (1 + \bar{p}_{GC} - \bar{p}_{IV}) - (\bar{p}_{IV} - vc) + r\bar{p}_{GC} \\ &\Rightarrow \bar{p}_{IV}^{*\bar{\alpha}=1}(\bar{p}_{GC}) = \frac{1 + vc + (1 + r)\bar{p}_{GC}}{2} \end{aligned} \quad (3.18)$$

and

$$\begin{aligned}
 \max_{\bar{p}_{GC}} \bar{\Pi}_{GC}^{\bar{\alpha}=1} &= (\bar{p}_{GC} - r\bar{p}_{GC} - vc)(\bar{p}_{IV} - \bar{p}_{GC}) \\
 &\Rightarrow 0 = (1 - r)(\bar{p}_{IV} - \bar{p}_{GC}) - ((1 - r)\bar{p}_{GC} - vc) \\
 \Rightarrow \bar{p}_{GC}^{*\bar{\alpha}=1}(\bar{p}_{IV}) &= \frac{(1 - r)\bar{p}_{IV} + vc}{2 - 2r}.
 \end{aligned}$$

These prices maximize the respective profits since $\frac{\partial^2 \bar{\Pi}_{IV}^{\bar{\alpha}=1}}{\partial \bar{p}_{IV}^2} = -2 < 0$ and $\frac{\partial^2 \bar{\Pi}_{GC}^{\bar{\alpha}=1}}{\partial \bar{p}_{GC}^2} = -2 + 2r < 0$ for $r < 1$. The mutual optimal prices are

$$\begin{aligned}
 \bar{p}_{IV}^{*\bar{\alpha}=1}(r, vc) &= \frac{2 + 2vc - 2r - vc \cdot r}{3 - 4r + r^2} \\
 \bar{p}_{GC}^{*\bar{\alpha}=1}(r, vc) &= \frac{1 + vc(3 - r) - r}{3 - 4r + r^2},
 \end{aligned}$$

and for $r = 0$ they become $\frac{2}{3} + vc$ or $\frac{1}{3} + vc$ for IV and GC , respectively. The total royalty effect on the optimal price for GC thus is $\bar{p}_{GC}^{*\bar{\alpha}=1}(r, vc) - \frac{1}{3} + vc$. The cost amplified royalty effect (RE_{vc}) and the competition amplified royalty effect (RE_{comp}) can be separated as follows

$$\begin{aligned}
 RE_{comp} &= \bar{p}_{GC}^{*\bar{\alpha}=1}(r, 0) - \bar{p}_{GC}^{*\bar{\alpha}=1}(0, 0) \\
 RE_{vc} &= \bar{p}_{GC}^{*\bar{\alpha}=1}(r, vc) - RE_{vc} - \bar{p}_{GC}^{*\bar{\alpha}=1}(0, vc),
 \end{aligned}$$

which are visualized in figure 3.6. Note that the competition amplified royalty effect RE_{comp} in % only changes in vc since the ratio is based on $\bar{p}_{GC}^{*\bar{\alpha}=1}(r = 0, vc)$, while absolutely it is independent of vc . The Figure 3.6 demonstrates that RE_{comp} can be of some significance compared to RE_{vc} for lower vc .

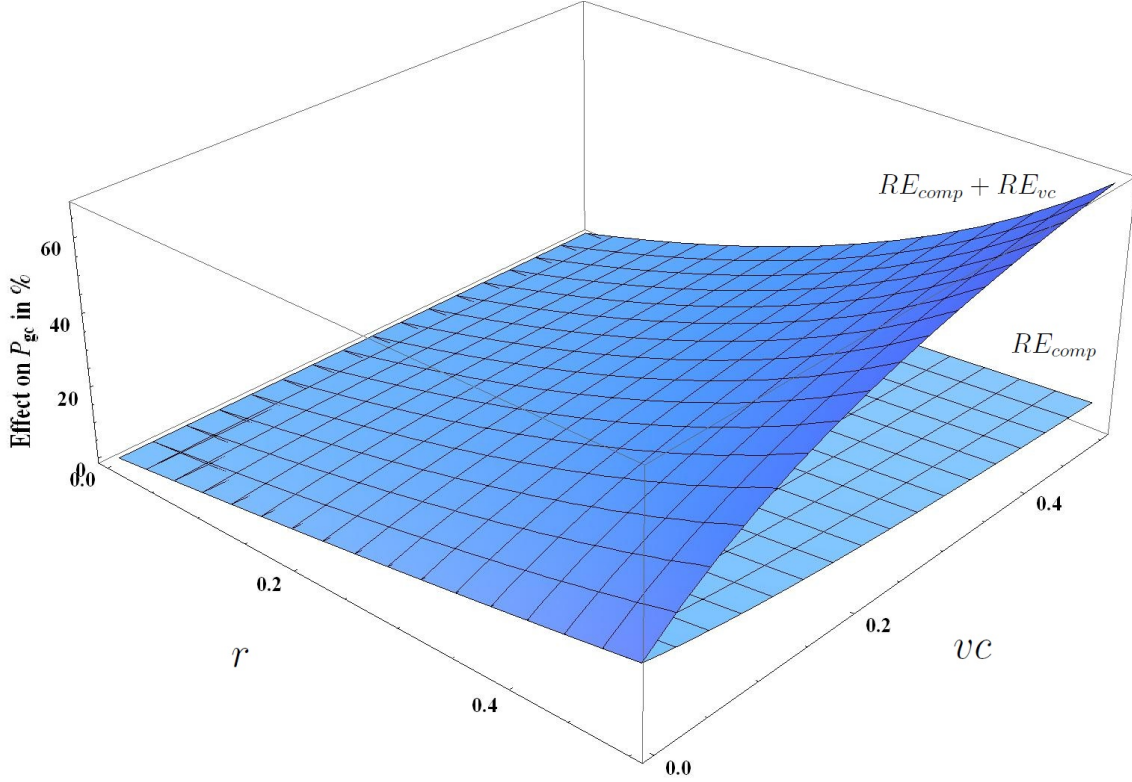


Figure 3.6.: Separated effects of royalty on generic price RE_{comp} and $RE_{comp} + RE_{vc}$ in % of $p_{GC}^{*\bar{\alpha}=1}(r=0, vc)$ for $r \in [0, 0.5]$ and $vc \in [0, 0.5]$.
hold.

3.4. Conclusion

The foregoing chapter detailed the framework of global Intellectual property rights and introduced the compulsory licensing (CL). While being obliged to grant patent protection for new medicines a government can introduce a competitor by utilizing CL. This measure is supposed to drive down prices and thus increase access. Before exploring the impact on incentives for research and development (R&D) in an international environment this chapter focuses on the static impact in a closed economy without dynamics. We explore the question on how the duopoly will unfold if compulsory licensing is issued. For this purpose we highlight the characteristics of drug demand in developing countries, depict a model which is later used to illustrate

findings and analyze the effects of remuneration on generic pricing.

Since drug payments are mostly out of the pocket, quality and price play an important role in the consumer's decision about purchasing drugs in developing countries. Further, multinational innovators might have a disadvantage on distribution networks, especially when it comes to neglected diseases (ND). To capture these effects a discrete asymmetric duopoly model is introduced which demonstrates that the innovator (IV) will be able to keep some profits in case of compulsory licensing, contrary to a Bertrand duopoly scenario. Additionally, the generic competitor (GC) will most likely be able to cut a share of profits due to the vast distribution network. How the duopoly manifests strongly depends on the type of disease and its socioeconomic prevalence. Further, the optimal price of the generic competitor is likely to be determined by factors outside of this duopoly situation such as negotiations and government control.

When turning to the remuneration we find that almost all countries applied a small royalty by net sales when issuing compulsory licensing. Such net sales based royalties unfortunately have the side effect of increasing the licensee's price, amplified by the costs. While this single effect might be negligible, competition further amplifies the royalty effect on the licensee's generic price, which is not accounted for in economic literature.

While these effects are demonstrated in the discrete asymmetric duopoly model the deployed assumption on demand is exemplary only. The developed discrete asymmetric model demonstrates the specific drivers of demand in developing countries plainly. Yet, it is a theoretical construct that requires further refinement and testing. In this model IV does not have the option to increase its market by cutting price and extending the distribution network. Further research could bring more clarity

to the CL duopoly by refining and testing this model. For the purpose of applying data, estimating parameters and testing the basic conjunction the 2-dimensional approach depicted beginning of section 2.2 is favorable over the discrete model because it imposes less restrictions to the structure of demand.

As an outlook, GC will set the price p_GC based on circumstances outside of this system. To begin with, CL is usually flanked with government subsidies for GC and other measures to increase access to the specific treatment. For example the much praised "Brazil model" for AIDS treatment consist of the goal to provide free universal access to treatment paired with heavy utilization of CL, either by issuing or using CL as a threat in price negotiations (Nunn et al. (2007) p. 1805). A comparable effect on domestic generic manufacturers' demand and pricing decisions will have the 2012 so called "\$5.4 billion policy" of India. Patients will get free access to any generic drug in major city hospitals as well as the smallest rural clinic. This policy was enacted in July 2012 and is expected to unfold within 5 years (Reuters (2012c)). Further, if not government owned, GC has to apply for compulsory licensing and propose a price $p_G^A C$ to the government, which will remain fixed. Accordingly, p_GC is not determined via demand, but by GC's effort to convince the government of compulsory licensing and undercut potential competitors.

The implications of these mechanisms are left unsolved in this chapter and GC's price is assumed to be given externally. However, the results will serve as a base for the discussion of the bargaining that takes place between innovator, generic competitor and government. These negotiations about price, royalty and the utilization of compulsory licensing depend on the outcome of such duopoly as the next chapter will demonstrate.

The results on royalty are general and represent a disadvantage of the compulsory

licensing instrument as used today. Chapter 6 will address the royalties again and investigate the effects in an international environment with cross border compulsory licenses. It will become apparent that least developed countries dependent on drug imports face a disadvantage compared to middle income countries.

4. Dynamic Aspects: Incentives

In the preceding chapters we briefly described the context of global patent protection and introduced the concept of compulsory licensing (CL) which each member of the World Trade Organization (WTO) is allowed to make use of. It permits a country to allow a generic manufacturer the production and marketing of a patented drug and effectively transform a patent monopoly into a duopoly. This duopoly is not perfect and the resulting prices are most likely not at marginal cost level. The innovator enjoys a perceived quality advantage while the domestic licensee can deploy a wide distribution network and reach rural areas the innovator cannot. While these results are based on static duopoly analysis we now turn to the dynamic aspects in a closed economy before dismissing this last restriction in chapter 6.

The word dynamic derives from the Greek $\delta\upsilon\nu\alpha\mu\iota\varsigma$ (dynamis) and means power, yet today is often used to express change. Accordingly, a dynamic system refers to a system in which parameters change over time. Similarly, dynamics in the economic context aim to capture the influence of time in a model. There are two main dynamic elements of compulsory licensing. It constitutes an interference with the patent system and the question arises if it has an effect on incentives. This aspect of dynamics is discussed in this chapter. Further, all compulsory licensing episodes identified in chapter 2 are preceded by negotiations. We address the question which

effect these negotiations have on the usage of compulsory licensing and its outcome in the next chapter 5.

At first we focus on the incentives induced by a patent system and elaborate the concept as analyzed by Arrow (1962). Thereupon we look at the weaknesses of patent systems in particular related to research for medications. The second part of the chapter briefly discusses mechanisms proposed in the economic literature that aim to foster private research and development (R&D) activity for neglected diseases. In this context we discuss Patent Buyouts (Kremer (1998)), Health Impact Fund (Hollis and Pogge (2008)) and last but not least Advanced Market Commitments (Kremer (2001)).

4.1. Incentives for Pharmaceutical Research

Generally, there are two monetary ways to leverage and incentivize innovation from a governments perspective. While one way is to fund research projects or reduce its costs directly ("push"), an indirect way is to create prizes for successful innovations ("pull"). While a pull incentive includes concrete prizes for inventions it also envelopes the expectation of future sales in wealthy markets, in particular by means of patents. Grace and Kyle (2009) explain that push and pull mechanisms are usually implemented together in many sectors, especially with regard to pharmaceutical research. While there are many directly funded institutions, pharmaceutical companies invest in research and are driven by expectations on exclusivity. Pull incentives deflect the risks of research failure to the private sector, because they reward results only. The other side of the coin is a possible wasteful duplication of research effort. The following will briefly outline the economic theory around patent protection and

point out a number of general problems coming along with this system.

4.1.1. Economics of Patents

Arrow (1962) formalized a system which models the incentive to innovate in a groundbreaking essay. He drew a comparison between monopolistic and competitive markets for process innovation. An important finding is that the incentive exceeds for a competitive market structure, irrespective the production cost advantage gained by the innovation.

In Arrow's model a process innovation per definition reduces the constant cost per unit from \bar{c} to $\underline{c} < \bar{c}$.¹ This approach can also be interpreted as product innovation, which is described later.

In a monopolistic market the innovator is defined to gain the profit $P(\bar{c})$ before and $P(\underline{c})$ after the innovation. This corresponds to the optimal monopolistic prices $p_m(\bar{c})$ and $p_m(\underline{c})$ as well as the resulting output $x_m(\bar{c})$ and $x_m(\underline{c})$, respectively. On the one hand the incentive to innovate in a monopolistic situation is $P(\underline{c}) - P(\bar{c})$. On the other hand this equals the change in marginal revenue $R(x)$ adjusted by the change in production costs:

$$P(\underline{c}) - P(\bar{c}) = \int_{x_m(\bar{c})}^{x_m(\underline{c})} R(x)dx - (\bar{c}x_m(\bar{c}) - \underline{c}x_m(\underline{c})). \quad (4.1)$$

A competitive framework is defined by zero profits with pricing at marginal costs prior to the innovation. Arrow distinguishes two situations: In case of $p_m(\underline{c}) < \bar{c}$ (drastic innovation) the innovator would demand a royalty $r = p_m(\underline{c}) - \underline{c}$ from

¹Arrow (1962)'s notation of costs aligned with Tirole (1988) to simplify matters when it comes to the welfare analysis (Tirole (1988) p. 391)

competitors to use the innovation and the incentive to innovate is $P(\underline{c})$. In the case of $p_m(\underline{c}) > \bar{c}$ (non-drastic innovation) the optimal royalty for the innovator would be $r = \bar{c} - \underline{c}$ so that the price remains at \bar{c} and thus the innovator's revenue equals $x_m(\bar{c})(\bar{c} - \underline{c})$.

Clearly, the incentive to innovate from a monopolists point of view ($P(\underline{c}) - P(\bar{c})$) is less than in a competitive framework ($P(\underline{c})$) for drastic innovations ($p_m(\underline{c}) < \bar{c}$). For a non-drastic innovation ($p_m(\underline{c}) > \bar{c}$) consider equation 4.1 with $R(x)$ decreasing in x . The monopoly output before invention $R(x_m(\bar{c}))$ is defined by the optimal choice $R(x_m(\bar{c})) = \bar{c}$. Accordingly,

$$\begin{aligned} & \int_{x_m(\bar{c})}^{x_m(\underline{c})} R(x)dx < c(x_m(\underline{c}) - x_m(\bar{c})) \\ \Leftrightarrow & \int_{x_m(\bar{c})}^{x_m(\underline{c})} R(x)dx - ((\bar{c})x_m(\bar{c}) - \underline{c}x_m(\underline{c})) < \bar{c}(x_m(\underline{c}) - x_m(\bar{c})) - (\bar{c}x_m(\bar{c}) - \underline{c}x_m(\underline{c})) \\ \Leftrightarrow & P(\underline{c}) - P(\bar{c}) < (\bar{c} - \underline{c})x_m(\underline{c}) < (\bar{c} - \underline{c})x_c(\bar{c}), \end{aligned}$$

for a declining demand curve and thus $x_m(\underline{c}) < x_c(\bar{c})$ since $p_m(\underline{c}) > \bar{c}$.

Hence, the incentive to innovate in a perfect competitive scenario exceeds the incentive for a monopolist ($V_m < V_c$). The previous monopolist's revenue acts as an inhibitor for research for both, drastic and non-drastic innovations.

The above formalized incentives to innovate can be interpreted as a product innovation for $\bar{c} = \infty$ with $P(\bar{c}) = 0$ and $x(\bar{c}) = 0$. Accordingly, a distinction between monopoly and competition situation is not required and a product innovation is always drastic ($p_m(\underline{c}) < \bar{c}$). However, a product innovation in a field might replace the companies prior profits with an inferior product. Accordingly, the differentiation between competition and monopoly before the innovation is of relevance. The incentive to innovate thus equals $P(\underline{c}) = 0$ and is grater than or equals the incentive

of process innovation.

Arrow (1962) additionally compares the desirable social benefit to the incentive for an innovator and argues that it always exceeds. The approach is to compare above described incentives with the consumer's welfare gains a social planner would achieve when pricing at production costs after innovation.

With regards to a process innovation, the analysis is separated by monopolistic and competitive situation as well as drastic ($p_m(\underline{c}) < \bar{c}$) and non-drastic innovation ($p_m(\underline{c}) > \bar{c}$).²

In case of drastic innovation in the competitive scenario the consumer's benefit increases, whereas for non-drastic innovations the price remains fixed at \bar{c} and only the innovator benefits. Taking into account that the incentive to innovate in a competitive situation is always higher than a monopolist's incentive ($V_m < V_c$) indicates a major invention not being profit maximizing while socially desirable.

Formally consider the monopolist's additional revenue due to the invention as

$$V_m = \int_{\underline{c}}^{\bar{c}} D(p_m(c))dc.$$

A social planner would set the price after the invention to \underline{c} . Hence the additional social surplus equals

$$V_s = \int_{\underline{c}}^{\bar{c}} D(c)dc,$$

and since $p_m(c) > c$ it follows that $V_m < V_s$ due to the underproduction of the monopolist.

²For this and the following see Tirole (1988) p. 391 et seqq., with the interest rate being suppressed ($r = 1$).

In a competitive scenario for a non-drastic innovation the price would remain fixed at \bar{c} and the incentive is

$$V_c^{ND} = (\bar{c} - \underline{c})D(\bar{c}) = \int_{\underline{c}}^{\bar{c}} D(\bar{c})dc,$$

whilst for a drastic innovation

$$V_c^D = (p_m(\underline{c}) - \underline{c})D(p_m(\underline{c})) = \int_{\underline{c}}^{p_m(\underline{c})} D(p_m(\underline{c}))dc.$$

From the consumer's demand $D(\bar{c}) < D(c)$ we get $V_c^{ND} < V_s$ and $p_m \underline{c} < \bar{c}$ (drastic innovation) yields $V_c^D < V_s^D$.³ Summarizing, the socially desirable incentive is neither attained by a monopoly nor by a competitive patent situation and the competitive incentive always exceeds the monopolist's, so that $V_m < V_c < V_s$.

The incentive induced by product innovation does also not match the socially desirable. A product innovation is always drastic, but further assume that the innovator does not replace a profit generating prior product. The incentive then equals $V_c^D = (p_m(\underline{c}) - \underline{c})D(p_m(\underline{c}))$ and as such lacks the consumer's benefit. Additionally, the incentive induced by product innovation is inferior due to the problem of monopolistic underproduction.

An analysis of patent systems is very complex and in particular the incentives for R&D are subject to a plurality of mechanics and effects. Tirole (1988) emphasizes that a judgment on the welfare effects of patent systems cannot be finalized as important aspects are yet to be explored.

³One can also see here as shown above: Given that $D(\bar{c}) > D(p_m(c))$ for all $c \geq \underline{c}$ in a non-drastic situation ($\bar{c} < p_m(\underline{c}) \leq p_m(c)$), clearly $V_m^{ND} < V_c^{ND}$. Additionally considering $V_m^D = (p_m(\underline{c}) - \underline{c})D(p_m(\underline{c})) - (p_m(\bar{c}) - \bar{c})D(p_m(\bar{c}))$ gives the same argumentation as above ($V_c^D = P(\underline{c}) > V_m^D = P(\underline{c}) - P(\bar{c})$) and $V_m < V_c$ always.

Comparing the incentive induced by a patent system with the socially desirable incentive shows, that it is subject to a variety of distorting effects. The analysis above explains why the incentive generated by a patent system is generally inferior to the welfare effect a social planner could achieve. On the contrary, this incentive might excess, as the innovator does not internalize the competitor's profit losses suffered from the innovation (Scherer (2007) pp. 41-43). Non generic "me-too" drugs do not provide any significant treatment advantage but bypass the patent. Such products as well as patent races might lead to a cumulated over-investment into research, as well. Tirole (1988) names these the appropriability effect (inhibiting effect on incentive) and the business stealing effects (excess effects on incentive).

4.1.2. Patent Critique & Industrial Drug Development

With particular regard to drugs, another group of incentive deforming effects unveils of which some entail additional negative properties. If patent enforcement leaks, anticipated counterfeits would reduce the incentive to innovate. In the worst case such counterfeits could also be dangerous for consumers: A "random mixtures of harmful toxic substances" or "inactive, ineffective preparations" could "result in treatment failure or even death" (World Health Organization (2010a)). This predominantly affects developing countries as patent enforcement is particularly weak (Hollis and Pogge (2008), p. 85).

An aspect introduced as the "Tragedy of the Anticommons" by Heller and Eisenberg (1998) indicates deficient incentives, but moreover complicates the administration of medications. Initially, Heller and Eisenberg (1998) argued against the privatization of bio-medical research during the 1980s and provided a refutation to the "Tragedy of the Commons", Hardin (1968). The innovation inhibiting effect arises from the

anticipated high costs of getting "access to multiple patented inputs to create a single useful product" (Heller and Eisenberg (1998), p. 699), which are boosted by strategic behavior as well as transaction costs. Multiple administrations of diverse substances, patented by different innovators, can prove cumbersome and costly for patients in developing countries with an inadequate health care distribution grid. In fact, this effect of patent protection could be an additional reason for compulsory licensing and alternative mechanisms for developing countries.

The incentive for R&D with regard to communicable diseases lacks another important component, since the treatment of such diseases does not only help the infected patients. It has a positive effect on not yet infected patients and supports the containment of the disease. These externalities are not included in the private valuation of a consumer and not monetarily rewarded to the innovator.

In the absence of any obligatory state health insurance, for example in developing countries, two critical and serious problems arise. Firstly, it is not possible to perfectly price discriminate and a uniform price will hinder access for the poor population. Furthermore diseases that affect predominantly the poor will not be sufficiently reflected by the incentives induced by patents. Both these problems require a closer look and are further discussed below.

Intellectual property rights are at the times a driving factor in many industries and range from copyrights over trademarks to patents and more. Patents are mainly filed in computer technologies, electrical machinery and pharmaceuticals as well as medical technology today (World Intellectual Property Organization (2011), p. 76 and Table A.7.1.1). Scherer (2007) demonstrates the density of research and development (R&D) in pharmaceuticals by considering the R&D/sales ratio, which is extraordinary high. He identifies several reasons why a reliable patent protection

feeds the unusual high private spendings in pharmaceutical R&D to a larger extend than in other industries.

Firstly, the costs required to reach a marketable product are very high as the outcome of research is highly uncertain and regulations are stringent for good reason, especially for ethical drugs. The process towards a new drug can be divided into five stages, starting with the pre-clinical attempt to isolate molecules with promising mechanisms of action. Such will be tested on animals and pursued further in search of a formulation adequate for testing on humans. If permitted, the substance can enter the first of three clinical trial phases with a small group of subjects. Going on, in Phases II and III the group of subjects is widened and especially blinded tests are conducted. This means that at least two panels of patients are considered which either take the new drug or are administered with a placebo or alternative drug. The goal is to identify safety of the drug, tolerance with patients and the efficacy to treat the targeted disease. Marketing approval for specific indications depends on this drug profile and is decided upon by relevant institutions such as U.S. Food and Drug Administration. In most cases the testing continues in so called Phase IV studies. These further determine the profile given the patients health condition or focus on extending the indications. At each of these stages a failure of new substance is likely. Especially at late stages such a failure is very costly, since much has been invested during the earlier stages.

Secondly, imitation is relatively cheap. Given the above described multiple research stages and keeping in mind that failure might take place even at the late stages the development of substance with known properties is not risky. Additionally, manufacturers of a generic drug are not obliged to satisfy the same approval criteria as the original drug and pass the three clinical stages, irrespective of biological drugs and biosimilars.

4.2. Alternatives

As we have seen above there are two sides to the coin of a general patent mechanism. Patents create incentives for innovation, but these incentives do not fully reflect the social need, especially with regards to the enhancement of already patented innovations. Additionally, the problems of patent race, reverse engineering and Anticommons intensify the ineffectiveness of the regime. Apart from the push approach to fund research directly there are numerous proposals for alternative pull mechanisms of which we discuss a selection below.

4.2.1. Patent Buyout Mechanism

A possible way to address some pitfalls of patent protection is to use so called patent buy-outs. For this purpose Kremer (1998) designs a mechanism that does not violate the innovators property rights and makes the bidders reveal their valuation of the monopoly value. The real private value of an invention is difficult to determine, but bidders in a sealed-bid second-price auction are assumed to obtain at least some information about the private value of the invention.

Thereafter either the government will buy-out the patent at a certain markup to the observed private value, or the highest bidder purchases the patent with a small probability p . Therewith the bidders have an incentive to reveal their valuations and the markup by the government is chosen to reflect the typical ratio between the social and private value of an invention. Kremer (1998) suggests a markup of at least two, based on empirical estimates which find a social return on R&D ranging from 50% to 270%. Even though the markup will most likely not meet the real social value it is generally a better estimation of it than the private value. This markup is

of some importance for the mechanism as will be depicted below.

However, this mechanism encounters a couple of problems that Kremer (1998) addresses and which will be depicted in the following. Obviously the inventor might have an information advantage, but additionally anticipated buy-outs could inhibit current research. The effects of an inventors production costs advantage, which Kremer (1998) discusses, are ignored here since with regards to drugs production costs are relatively small.

Adverse Selection Even though the potential bidders for the patent are mostly competitors in the pharmaceutical market, they are likely to only have a fraction of the innovators information available and valuations will thus differ. For example they could understand the true value of the patent being distributed uniformly between a lower and upper bound L and U . If the bid B wins and the patent is sold at the price B then the upper bound of the true private value becomes $\min(U, B)$ and a classical adverse selection problem shuts down the market.

If the government offers a markup M , the bidder does not want to win with $MB > U$, conditional on winning with the bid B , so that in equilibrium

$$B = L + \min(U, MB)/2,$$

which implies

$$B = \min\left(\frac{L+U}{2}, \max\left(0, \frac{L}{2-M}\right)\right).$$

The adverse selection thus is reduced by the markup, even in cases other than uniformly distributed valuation.

Effects on Research

Kremer (1998) identifies and addresses a couple of incentive problems possibly induced by a patent buy-out mechanism. Referring to models of creative destruction Kremer argues that anticipated future research, which is subsidized by a patent buy-out mechanism, leads to overall less research, as depicted below. Contrariwise, complementary drugs would have an research increasing effect and patent buy-outs for durable goods would lead to anticipated low future prices. Complements as well as durable goods are rare in the pharmaceutical industry and thus not considered in the following (Kremer (1998) pp. 36). Consider two complementary drugs A and B , bidders (e.g. A) will anticipate that the other patent (B) is likely to be bought out by the government and is put into the public domain. The private as well as social value of the non public drug (A) is thus anticipated to be higher according to the complement characteristics.

Subsidy Effect: Let x_t be the investment in R&D at time t depending on the subsidy to research M_t so that $x_t(M_t)$, with $\frac{\delta x_t}{\delta M_t} > 0$, and assume that future research inhibits current ($\frac{\delta x_t}{\delta x_{t+1}} < 0$). The steady state of this system x^* naturally increases in a constant markup M but less than when considering just one period. The envelope theorem gives the total derivative

$$\begin{aligned} \frac{\delta x_t^*}{\delta M_t} &= \frac{\delta x_t}{\delta M_t} + \frac{\delta x_t}{\delta x_{t+1}} \frac{\delta x_t^*}{\delta M_t} \\ \Leftrightarrow \frac{\delta x_t^*}{\delta M_t} &= \frac{\frac{\delta x_t}{\delta M_t}}{1 - \frac{\delta x_t}{\delta x_{t+1}}} \\ \Rightarrow \frac{\delta x_t^*}{\delta M_t} &< \frac{\delta x_t}{\delta M_t}, \end{aligned}$$

since the future research inhibits current ($\frac{\delta x_t}{\delta x_{t+1}} < 0$). In other words: Let x^s be the socially optimal investment in R&D with the markup M^s solving $x^s = \Phi(M^s, x^s)$ and equivalently denote x^p as the investment in research in the absence of patent buy-outs. M^s as well as M^p (with $x^s = \Phi(M^p, x^p)$) also reflect the ratio between the social and the private value in a social planners or non buy-out Patent mechanism. Assuming that $x^s > x^p$ and since $\frac{\delta \Phi}{\delta x} < 0$ in order to reach the optimal $x^s = \Phi(M^s, x^s) = \Phi(M^p, x^p)$ the socially optimal markup M^s exceeds the ratio M^p of the patent framework without buy-outs.

Substitute Effect: Additional to the inhibitive effect of patent buy-outs on current research due to its subsidizing nature on future competition, it is likely to be put in public domain in such a regime. Kremer (1998) clarifies this second inhibitive effect by means of the basic inventor and follower model. Suppose that I and C are the costs of invention and copy and the values of monopolistic and duopoly return are S and D , respectively. Following an invention is worth it if $D > C$ and invention pays off only for $I < D$, compared to $I < S$ if there will be no follower ($D < C$).

Consider the game tree in figure 4.1 for the game of inventor and follower in a patent buy-out mechanism, in which the two are bought-out with a markup M on the bids $B(F)$ as well as $B(I)$ and are randomized successively. Private bidders value the follower by the duopoly payoff D and accordingly the following drug is invented if $MD > C$. In the case of the follower being bought out publicly, the leading drug is worth 0 so that bidders only bid pD . Thus, invention of the leading drug is inhibited if a follower is anticipated ($MD > C$) and invention costs exceed the marked up expected payoff in this situation ($MpD < I$).

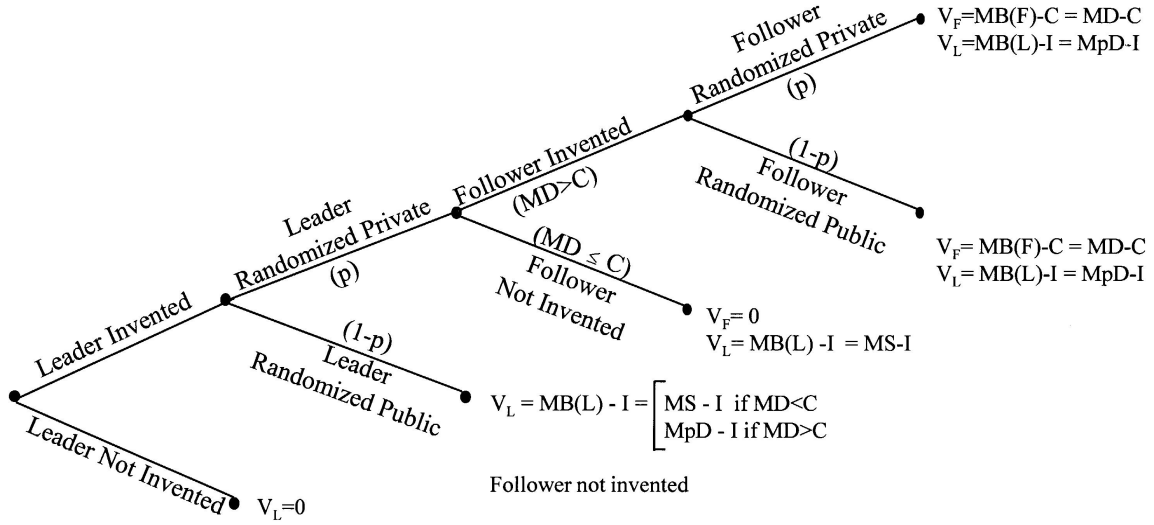


Figure 4.1.: Patent buy-outs with follower but without joint randomization. Picture from Kremer (1998) "Patent Buyouts: A Mechanism For Encouraging Innovation", p. 29f..

Joint Randomization:

As a possibility to address the above depicted innovation inhibiting effect Kremer (1998) suggest to let the government buy-out and randomize the two patents jointly after the follower enters. See figure 4.2 for Kremers joint randomization proposal and note that bidders bid for each patent separately. Both patents are either sold to the 2 winners auctions together or put in the public domain, whereas the markup for the leader is not payed again if it already went through a buy-out. Identifications of substitutes or ratings are not necessary, since jointly randomization with a non substitute does no harm. In this joint randomization process bidders value each patent by D , the government will buy-out at MD and thus the follower (leader) invents if $MD > C$ ($MD > I$). For $D > C$ and $MD < C$ the depicted mechanism increases incentives for research. Without buy-outs (compared to joint randomization) the incentive to innovate for $D > C$, so that a follower enters, is $D - C$ (compared to $MD - C$). If there is no follower in either mechanism ($MD < C$) the incentive would

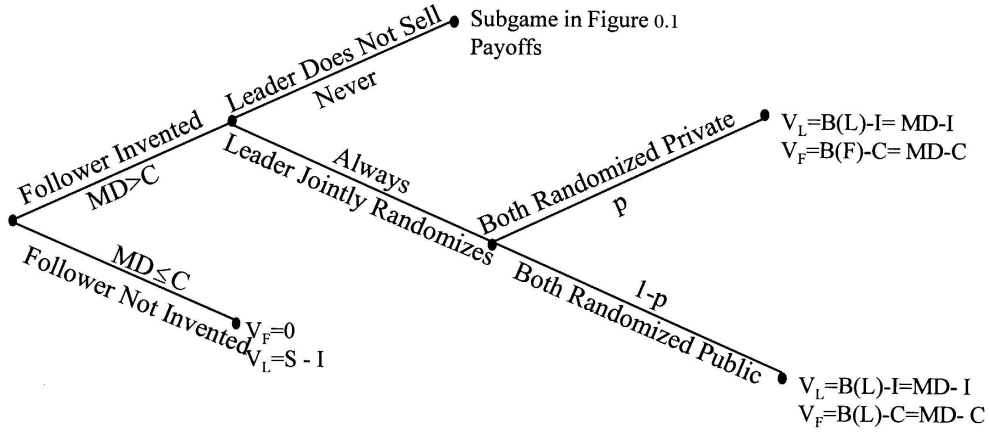


Figure 4.2.: Patent buy-outs with follower and joint randomization. Picture from Kremer (1998) "Patent Buyouts: A Mechanism For Encouraging Innovation", p. 31f..

be $S - I$ (compared to $MS - I$).

Only if the buy-out mechanism induces a follower which would not follow otherwise ($D < C < MD$) and $MD < S$, it gives less incentives since the leader invents when $MD > I$, compared to $S > I$ in the conventional mechanism. However, this exception is based on the assumption of one follower only, since another would reduce the incentive to develop the first follower, etc..

Collusion and Ceiling Prices

In the above depicted patent buy-out mechanism an inventor could bribe a bidder to increase the bid. The buy-out prize would increase, but the bribed bidder only had to pay the bid by chances of p . Apart from the general provisions to prevent collusion such as sealed bids, even after the auction, Kremer (1998) suggests some approaches of which so called "ceiling prices" are highlighted in the following.

For example a third price auction could increase the bribing effort. Additional op-

tions are the possibility to cancel randomization, forcing innovators to provide information about ties with an auction winner as well as the requirement for bidders to pay a licensing fee. Additionally the commissioned government agency will not be able to buy-out all patents due to a restricted budget and thus could choose not to buy-out those patents with an abnormal high prize.

Apart from conventional ceiling price mechanism e.g. based on a multiple of prior buy-out sales, Kremer (1998) draws attention to a configuration of the above depicted patent buy-out mechanism. Given the randomization to a private bidder with probability p the innovator would not receive any payment if the patent is bought out, but $\frac{M}{p} \min(bid, \pi)$, with π denoting the realized profits, in the case of private randomization. The expected payoff thus is $M \min(bid, \pi)$ and could be guaranteed by an insurance. The innovator would have to additionally and permanently bribe the winner in order to subsidize its sales and achieve the bid times the markup.

4.2.2. The Health Impact Fund

A promising mechanism is the "Health Impact Fund" (HIF) as its support grows and does not require modifications on current patent legislation. The HIF, developed by Hollis and Pogge (2008) and promoted by the non-profit organization "Incentives for Global Health", has drawn worldwide attention and is supported by academics, politicians and non-governmental organizations. For example an HIF pilot is supported by the World Health Organization as well as the Social Democratic Party of Germany (Social Democratic Party of Germany (2010)).

An important advantage of the HIF is that registration of products with the HIF is optional for the innovator. For approval, the innovator has to hold a patent, commit

to a low price at marginal costs of production and preauthorize the HIF to achieve market clearance by means of sublicensing generic companies. Furthermore, the HIF can deny registration if the product is not suitable. In return, a registrant will receive an annual payment for ten years.

A proposed reward concept is to grant an innovator a share of the fixed annual HIF payout based on the contribution to global health. The health impact assessment required for that purpose is the crucial element of the HIF mechanism, while at the same time a criticized weaknesses. Estimation of the incremental health impact is a very complex task, "but the alternative is to reward innovators on the basis of ignorance" (Hollis and Pogge (2008), p. 9). Among others, the objectives are to account for an improved access due to lower prices, refined therapeutic profile as well as a reduction of infections caused by communicable diseases. In order to meet these high aims, a major part of the HIF institution would be dedicated to the continuous evaluation of health impacts.

In order to provide significant incentives, a long term commitment of substantial government funding is required. Hollis and Pogge (2008) suggest an initial amount of six billion dollars per year, segmented across countries according to their GDP. The participating countries would in return benefit from the reduced prices.

Critique on the HIF concept mostly addresses the health impact assessment. Estimating the incremental health impact is especially difficult due to the varieties in drug latency periods or the availability of data. Additionally, the costs required for this health impact assessment could be very high as a major part of the HIF institution would be involved. Hollis and Pogge (2008) argue that such an expensive assessment is required to provide incentives independent from wealth. Since participation in the HIF is optional, it does not directly influence monopoly profits. More

importantly it will attract drugs with relatively high health impact when distributed at marginal costs, than compared to the monopoly revenues. As Hollis and Pogge (2008) as well as Grootendorst (2009) depict, neglected diseases and those with large externalities like vaccines would benefit from this option.

4.2.3. Advanced Market Commitments

Kremer (2001) proposes another pull mechanism in order to accelerate private R&D investment in particular for vaccines targeting neglected diseases. This proposal was supported by publications from Kremer and Glennerster (2004), Barder, Kremer, and Williams (2006), Levine, Kremer, and Albright (2005) and Berndt et al. (2007), recommended to the Group of Eight (G8) as well as the Bill & Melinda Gates Foundation and piloted in 2007. The advanced market commitment (AMC) mechanism aims to address two dilemmas with regard to neglected diseases. First, time-inconsistent incentives could put prices of newly developed drug under pressure even though the respective government initially encouraged innovators to invest in R&D for vaccines. Since these time-inconsistencies are anticipated by innovators the incentive to invest diminishes. Second, governments face a free-riding problem as the benefits of novel vaccines take global dimensions. Accordingly, least developed countries (LDC) have little incentive to unilaterally fund such development (Barder, Kremer, and Williams (2006)). As depicted in section 6.1 these problems become in particular crucial for compulsory licensing, which is not considered in this way by the above authors, yet supports their reasoning.

Sponsors of AMCs would legally obligate themselves to purchase a novel drug which achieves a predefined target product profile (TPP). This purchase could be a full purchase commitment based on a predefined quantity of treated patients or to sub-

sidize low prices that poor countries would pay to reach a higher price. Subsequent to the purchase of the predefined quantity the innovator would be obliged to lower the price or license out the production to other manufacturers. The TPP defines a minimally acceptable profile, among others with regard to safety, vaccine serotypes or administration (*Target Product Profile (TPP) for the Advance Market Commitment (AMC) for Pneumococcal Conjugate Vaccines*, GAVI Secretariat (2007)). In

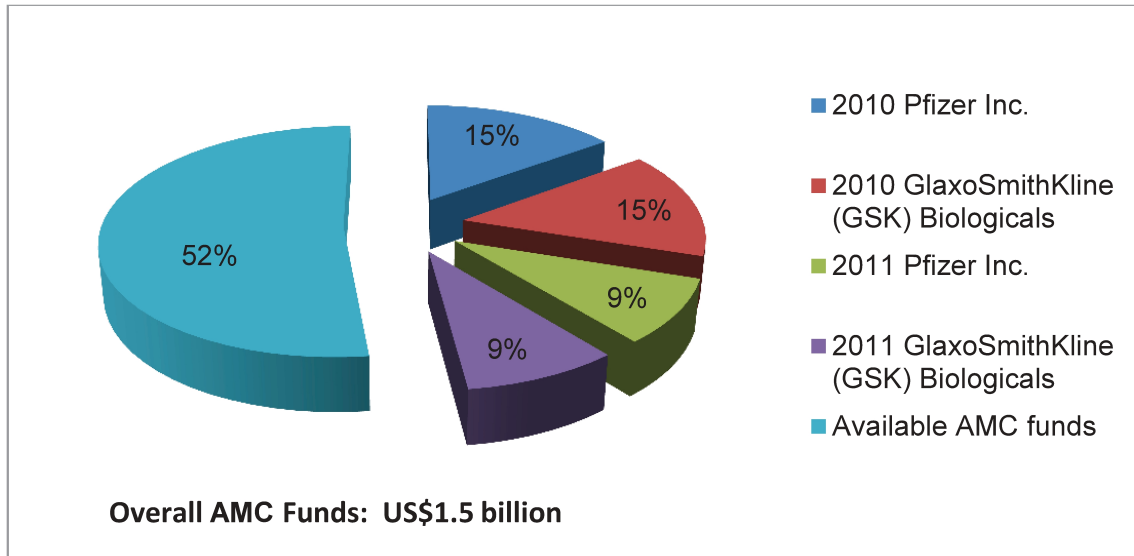


Figure 4.3.: Fund allocation of advanced market commitment pilot on pneumococcal vaccines in 2010 and 2011. The 52% remaining AMC funds are carried forward and enriched with the additional donation by end of 2011. The source of the graph is *Annual Report 2012: Advanced Market Commitments for Pneumococcal Vaccines*, GAVI Secretariat (2012) p.10.

2007 an AMC pilot on pneumococcal vaccines was started and the governments of Italy, United Kingdom, Canada, Russian Federation and Norway as well as the Bill & Melinda Gates Foundation pledged an initial total of 1.5 billion US\$ to the program (GAVI Secretariat (2013)). By 2011 the total resources to the AMC for the period of 2011 to 2015 rose to 7.6 billion US\$. The *Annual Report 2013: Advanced Market Commitments for Pneumococcal Vaccines* (GAVI Secretariat (2013)) details that to date 70% of the supported countries planned for the introduction of vaccines

provided by Pfizer and GlaxoSmithKline. Further, in 2010 as well as 2011 the initial funding of 1.5 billion US\$ was partially disbursed to these companies as figure 4.3 illustrates. Summarizing, the crucial element of advanced market commitments is the credibility of promised purchases to stimulate R&D.

4.3. Conclusion

Intellectual property rights aim to provide incentives for innovation. The economic rationale behind this concept is briefly outlined in this chapter, closely following Arrow (1962). The monopoly induced by a future patent provides high expected sales and in consequence encourages higher investments to succeed. Arrow (1962) compares this incentive with the investment a social planner would undertake and distinguishes between two starting points, a competitive and a monopolistic framework. Generally, the resulting incentive is inferior to the socially desirable and the incentive under prior competition exceeds the monopolist's.

There are numerous additional effects which influence the induced incentive and blur welfare assessment as Tirole (1988) points out. To name but a few the innovative competitor does not take into account the other competitor's losses due to his innovation. With regard to drugs it is difficult for regulators to assess which drug is novel and which a so called "me too", not providing any additional value. Heller and Eisenberg (1998) explain that valuable fix dose combinations of drugs are often not available due to the "Tragedy of the Anticommons", indicating costly collusion between multiple patent holders. Additionally, positive external effects of treating communicable diseases are neither considered by innovators nor rewarded by payers. Nonetheless Scherer (2007) points out how important time consistent patent protec-

tion is in particular regarding the development of pharmaceuticals, since drugs are easy to imitate yet risky to develop.

In the second half of this chapter we discuss selected alternative mechanisms which are designed to address some of the above diffusions.

Kremer (1998) suggest that governments buy out patents by means of an auction in which the private value is determined. The buyout offer is optional and only occurs with a fixed probability in order to give bidders an incentive to bid. While achieving high access via low prices there remains a probability of monopolistic manufacturers. The buy-out mechanism provides a solution to under investment in R&D, wasteful "me too" research and the deadweight loss due to monopolistic pricing. But the mechanism induces a couple of problems such as research inhibiting anticipated substitution effects as well as collusion. While Kremer (1998) suggest solutions to those and additionally comes up with the idea of purchasing funds with regards to developing countries later (Kremer (2002)), the political and practical feasibility is problematic (Tirole (2006)). Even though the patent buy out mechanism would increase accessibility in developing countries it seems difficult to implement, since the buy-out price and thus costs for a developing country's government exceeds even the private value of the patent. Currently, developing countries do not even grant this private value to innovators, considering compulsory licensing or the absence of any state health insurance. Additionally, implementation of such a system appears more difficult since just a decade ago "TRIPS" was agreed on and is even not yet enforce in some least developing countries. Although, feasible in developed countries the needed immense government discretion will be difficult to achieve in most developing countries.

With the "Health Impact Fund" (HIF) Hollis and Pogge (2008) suggests to reward

innovation directly paying annual prizes. To gain this payment an innovator must have licensed the HIF to pursue market clearance. The main difference to ordinary prize funds is that no target profile is set but the value of the innovation and thus the share of the fund payment is determined based on a health impact assessment. This assessment is also the main point of critique as it will be a very complex task requiring a costly evaluation.

For advanced market commitment (AMC) mechanisms proposed by Kremer (2001) sponsors commit to fully or partially purchase drugs that achieve a predefined target product profile. For the advanced market commitment to work the explicit financial commitments need to be credible. This mechanism is already being employed as a pilot on pneumococcal vaccines and two innovators developed products achieving the minimal target product profile. Advanced market commitments aim to correct time inconsistent developing country preferences in particular with regard to neglected diseases.

In the next chapter we will analyze the negotiations prior to compulsory licensing and depict why advanced market commitment are in particular relevant for compulsory licensing. Additionally, the depicted extensive game points out that negotiations are an essential price reducing tool for respective governments, applying for both, innovator as well as generic manufacture. In chapter 6 the restriction of a closed economy is relaxed and static as well as dynamic negotiations reassessed in this context.

5. Dynamic Aspects: Negotiations

We demonstrate in chapter 2 that the instrument of compulsory licensing (CL) is frequently considered for domestic application in developing countries. While some of these episodes result in an actual CL, others turn out to achieve a significant price reduction on the monopolistic innovator's (IV) price. If a compulsory license is granted a private generic competitor (GC) will optimize profits and most likely not price at production cost. We indicated in chapter 3 that for a static environment without negotiations the competition between innovator and domestic generic manufacturer is not perfect. Perceived quality differences and the domestic generic's distribution network advantage drive the generic competitive price, further increased by a royalty based on sales. The foregoing chapter 4 briefly introduced the economic concept of incentives based on patents and highlighted selected alternative or auxiliary mechanisms. This section will shed light on the dynamics of negotiations preceding CL. While the considerations on incentives are long term, the dynamic aspect of the CL negotiations simply roots in the sequence of price proposals and compulsory licensing decision. The question discussed in the following is how negotiations influence the outcome of CL considerations and understand the features induced by private generic manufacturers participating in these.

We investigate the negotiations between a country's government (G) and a multina-

tional pharmaceutical company, innovator (IV) henceforth, by means of an extensive game with perfect information. In particular, the innovator proposes a discounted monopoly price in anticipation of the government's decision about CL based on this price. Within this simple setup we simulate the actual observation that a significant portion of CL episodes end with a discounted innovator's price rather than issued CL. Further, chapter 4 points out that the long term dynamic aspect of patent protection leads to incentives for innovation. Since these incentives depend on the expected return it largely leaves out diseases predominantly affecting the poor, so called neglected diseases (ND). In a closed economy this problem might be aggravated by compulsory licensing usage. We find that a government is more likely to issue compulsory licensing for drugs indicated for the treatment of neglected diseases. If this was anticipated by an innovator the inferior incentive to develop medications for neglected diseases is diminished further.

Subsequently, the model is expanded to capture the aspect of a domestic generic manufacturer applying as a licensee of compulsory licensing. As a result the generic manufacturer pursues compulsory licensing by pricing low. This leads to a generic price either below or equal to the static duopoly pricing which could improve access to the treatment. While the general results of the analysis are carried forward the interaction of these players is subsequently demonstrated in an example. In particular the game is applied by utilizing the duopoly model derived in chapter 3 as an outcome.

Chapter 6 will pick up the dynamic negotiation game again and explain why a change in the sequence of moves as it is induced by the cumbersome process of cross border compulsory licensing will eliminate the effect of a reduced generic price.

5.1. Compulsory Licensing as a Threat

Before issuing a compulsory licensing, the country usually negotiates with the respective innovator (IV) about the drug's price. In practice such negotiations might lead to a discount on the original drug and the government refrains from CL . The upcoming will simulate this situation in form of an extensive form negotiation game with perfect information between a foreign research based pharmaceutical innovator (IV) and the government GC of the considered developing country.¹ Generally speaking, these two players have almost opposed preferences. While the innovator aims to maximize profits the government seeks to maximize consumer welfare, which is represented by minimizing full coverage costs.

In the considered dynamic negotiation game N of complete information and successive moves the players are given by $i \in N_N = \{IV, G\}$, namely innovator and government, respectively. Actions and order of moves are represented in the extensive form of N in figure 5.1. IV moves first and sets a positive price p_{IV} for the considered branded drug. Subsequently G has the option to issue compulsory licensing (cl) or not ($\neg cl$). Accordingly, the player function is given by $P(\emptyset) = IV$, $P(p_{IV}) = G$ and the actions at each stage are $A(\emptyset) = \{p_{IV} \in [0, \infty]\}$, $A(p_{IV}) = \{cl, \neg cl\}$. The set of histories H_N consists only of four elements \emptyset , p_{IV} , (p_{IV}, cl) , $(p_{IV}, \neg cl)$, including non-terminal histories. The set terminal histories of N after the second stage is $Z_N = \{(p_{IV}, cl), (p_{IV}, \neg cl)\}$. Whereas from (p_{IV}, cl) the game ends with the duopoly situation, it results in a monopoly with $(p_{IV}, \neg cl)$.

¹The following is a generalized model from Brebeck (2009).

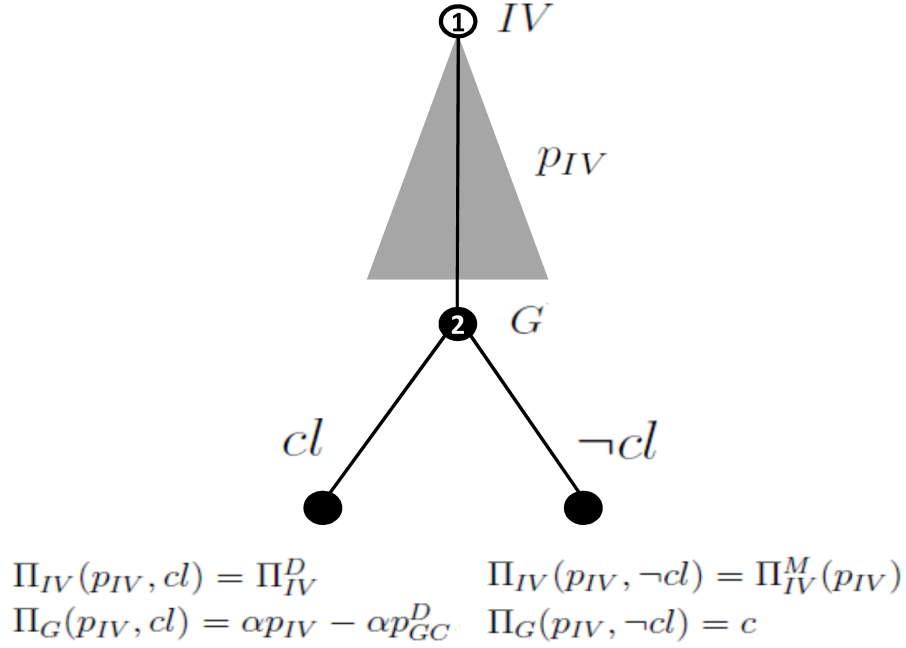


Figure 5.1.: Representation of extensive negotiation game N

For ease of interpretation the duopoly outcome is assumed as given and is not modeled as another subgame. The payoff-functions Π_{IV} and Π_G represent the innovator's and government's preferences, respectively, as a base for their decision. The innovator's revenue from monopoly is determined as $\Pi_{IV}(p_{IV}, \neg cl) = \Pi_{IV}^M(p_{IV})$, without going into details here. If the government chooses to issue a compulsory licensing, the innovator faces a duopoly situation represented by IV 's payoff $\Pi_{IV}(p_{IV}, cl) = \Pi_{IV}^D$.

In general, the government G focuses on welfare of domestic consumers. As a measurement for consumer welfare the government is assumed to consider compensating variation $cv(p_{IV}, p_{GC})$. This concept from Hicks (1942) measures the additional expenditure for consumers, given that they have to pay a higher price but still desire to reach the same utility level. Given an utility level u and expenditure function e one of Hicks (1942) definitions is $CV = e(p_0, u) - e(p_1, u)$, with p_0 and p_1 being the old and new prices, respectively. However, measuring consumer welfare regarding drug

price changes can be delicate due to serious consequences in (developing) countries without any state health insurance. If the expenses are paid out of consumer's pockets a price increase could mean access refusal for the poor population. While problematic, this concern can be avoided by altering the interpretation: Suppose the government is considering to pay the drug for all needy patients who cannot afford it. Following section 3.2 these consumers of type $\hat{\Theta}_{RA}$ are represented by α and G would have to buy the drugs for αp_{IV} . In case of compulsory licensing however, G only has to pay the generics competitor duopoly price αp_{GC}^D . Accordingly, the compensating variation is $cv(p_{IV}, p_{GC}^D) = \alpha p_{IV} - \alpha p_{GC}^D$.

Additionally, there are potential downsides of compulsory licensing from the government's point of view. By issuing compulsory licensing a government generally could discourage other companies and industries from engaging in foreign direct investment (Bird and Cahoy (2008)). Further, other countries might apply political pressure as it happened in various compulsory licensing disputes described in sections 2.2 and 2.3. These barriers are considered in the game N as aggregated cost of compulsory licensing $-c$.

Summarizing, the extensive form of game N is given by the

$$\begin{aligned} \text{set of players: } N_N &= \{IV, G\}, \\ \text{set of terminal histories: } Z_N &= \{(p_{IV}, cl), (p_{IV}, \neg cl)\}, \\ \text{player function: } &\left\{ \begin{array}{l} P(\emptyset) = IV \\ P(p_{IV}) = G \end{array} \right. \text{ and the} \end{aligned}$$

$$\text{preferences: } \left\{ \begin{array}{l} \Pi_{IV}(p_{IV}, \neg cl) = \Pi_{IV}^M(p_{IV}) \\ \Pi_{IV}(p_{IV}, cl) = \Pi_{IV}^D \\ \Pi_G(p_{IV}, \neg cl) = c \\ \Pi_G(p_{IV}, cl) = \alpha p_{IV} - \alpha p_{GC}^D. \end{array} \right. \quad (5.1)$$

The following will analyze the game by using backward induction in order to describe the set of subgame perfect equilibria. This concept is favorable over a Nash equilibrium in strategic form in this specific case as empty threats need to be ruled out, following Selten (1965). For example consider the government's strategy to issue CL every time IV prices above production costs and IV to give in. This would be a Nash equilibrium as no player can improve by deviating from their strategy. Yet, this outcome is not plausible since the government's rigorous threat is not reliable. The second stage subgame $N(p_{IV})$ after history (p_{IV}) deals with the government's decision whether to issue compulsory licensing (cl) or not ($\neg cl$). Consider the strategy $s_G^*|_{p_{IV}}$ within this subgame

$$s_G^*|_{p_{IV}} = \left\{ \begin{array}{ll} cl & \text{for } \Pi_G(p_{IV}, \neg cl) < \Pi_G(p_{IV}, cl) \\ \neg cl & \text{for } \Pi_G(p_{IV}, \neg cl) \geq \Pi_G(p_{IV}, cl) \end{array} \right.$$

The strategy $s_G^*|_{p_{IV}}$ is a Nash equilibrium for the subgame $N(p_{IV})$ since G cannot obtain a better outcome by deviating, given a price p_{IV} . It simply demands that G decides about compulsory licensing based on the outcome. If G prefers the outcome of CL given a price p_{IV} it will issue CL , otherwise not. When using the outcomes

defined in 6.4 $s_G^*|_{p_{IV}}$ can be written as

$$s_G^*|_{p_{IV}} = \begin{cases} cl & , \text{ for } c < \alpha p_{IV} - \alpha p_{GC}^D \\ \neg cl & , \text{ for } c \geq \alpha p_{IV} - \alpha p_{GC}^D. \end{cases} \quad (5.2)$$

Stepping back into the first stage of the game we look at the subgame $N(\emptyset)$ in which the innovator IV decides upon the price proposal p_{IV} . IV anticipates G 's strategy can influence the government's decision by altering p_{IV} . Consider the following strategy $s_{IV}^*|_{\emptyset}$. Do detain G from issuing CL IV sets the price just low enough at $p_{IV} = \frac{c}{\alpha} + p_{GC}^D$ according to 5.2. Further, IV will only convince G of not issuing CL if this is beneficial and decides based on the outcome. The resulting monopoly profit $\Pi_{IV}^M(p_{IV})$ with $p_{IV} = \frac{c}{\alpha} + p_{GC}^D$ is compared to the duopoly given by Π_{IV}^D . When using the preferences 6.4 this strategy $s_{IV}^*|_{\emptyset}$ can then be written as

$$s_{IV}^*|_{\emptyset} = \begin{cases} p_{IV} > \frac{c}{\alpha} + p_{GC}^D & \text{for } \Pi_{IV}^M(p_{IV}) \leq \Pi_{IV}^D \\ p_{IV} = \frac{c}{\alpha} + p_{GC}^D & \text{for } \Pi_{IV}^M(p_{IV}) > \Pi_{IV}^D, \end{cases} \quad (5.3)$$

and IV can not benefit from deviation. Accordingly, the strategy profiles $s_{IV}^*|_{\emptyset}$ and $s_G^*|_{p_{IV}}$ represent a subgame perfect equilibrium of the game N (Osborne and Rubinstein (1994)). For each of the two subgames no player can benefit by deviating given the other player's strategy.

In order to avoid a third case it is assumed that G is considering a CL at all. That is $\frac{c}{\alpha} + p_{GC}^D$ is always smaller than a monopoly optimal price before the CL negotiations.

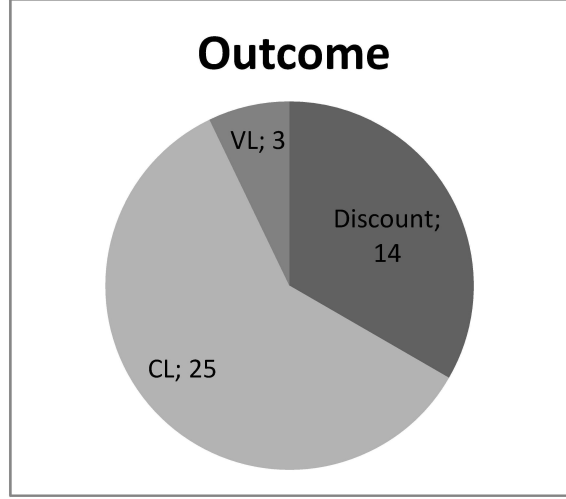


Figure 5.2.: Compulsory licensing episodes by outcome based on table 2.1

In words, the innovator could be able to avoid compulsory licensing by giving a discount. IV will do so unless the expected payoff from a duopoly situation exceeds the monopoly profit with discounts. In fact, a third of CL episodes between 2000 and 2012 resulted in discounts as figure 5.2 shows. For instance, consider the prehistory of compulsory licenses in Brazil depicted in section 2.2. Before issuing CL in 2007 the Brazil government was able to negotiate price discounts on several drugs between 40% and 65% already in 2001. Among all 43 CL episodes figure 5.2 and table 2.1 demonstrate that 14 negotiations were settled by discounts, at least for a while. Table 5.1 gives details of the CL episodes in table 2.1. While for the South African discounts no values are available, the remaining 8 examples show how significant these discounts are. The second aspect deducible from 5.3 is how the pressure on IV changes for diseases that affect predominantly the poor population α . If this

²Note that the preferences of government can also be written as $\Pi_G(p_{IV}, \neg cl) = c - \alpha p_{IV}$ and $\Pi_G(p_{IV}, cl) = -\alpha p_{GC}^D$ and yield the same results. However, the interpretation would be that the government will buy the drug from IV if no compulsory licensing is issued. This would also mean that the profit of IV becomes bigger due to the additional sales for consumers of type $\hat{\Theta}_{RA}$, measured by α .

Row	Episode Period	Nation	Molecule	IV	Discount
1	2001	Brazil	efavirenz	MERCK	60,0%
2	2001	Brazil	indinavir	MERCK	65,0%
3	2001	Brazil	nelfinavir	ROCHE	40,0%
4	2003	Brazil	atanazavir	BMS	76,4%
5	2003	South Africa	zidovudine	GSK	
6	2003	South Africa	stavudine	BMS	
7	2003	South Africa	didanosine	BMS	
8	2003	South Africa	efavirenz	BMS	
9	2003	South Africa	indinavir	MSD	
10	2003	South Africa	abacavir	GSK	
11	2006	Brazil	lopinavir	GILEAD	50,0%
12	2007	Brazil	atanazavir	BMS	7,0%
13	2007	Brazil	lopinavir	ABBOTT	3%-5%
14	2007	Thailand	Imatinib	NOVARTIS	100,0%

Table 5.1.: Compulsory licensing episodes with discount outcomes. The 100% discount (row 14) of Novartis on imatinip is restricted to households with income per year of less than 1.7 million baht only. Sources are Beall and Kuhn (2012a), Wetzler and Ayala (2008) and Wetzler and Palmedo (2008).

population increases IV is less likely to offer a price that would avoid compulsory licensing. Above all, the government can achieve the highest compensating variation for diseases that affect the poor population and is thus willing to accept the costs of compulsory licensing c easily. While this finding is in line with general understanding of a governments' objectives and thus induced by the assumption of compensating variation, figure 5.3 supports this as the majority of compulsory licensing episodes applies to HIV drugs. Additionally compulsory licensing for drugs is widely accepted and the costs c of utilizing CL might be lower. Another incentive for the government to issue compulsory licensing which is not factored in the compensating variation is the aspect of communicable diseases. By treating a communicable disease and containing a potential further spread future treatment costs are reduced.

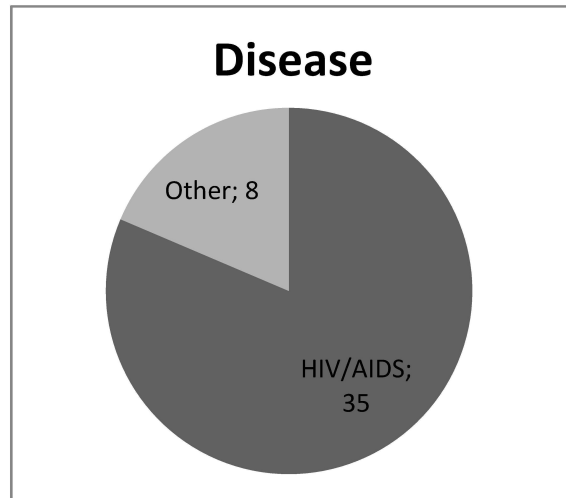


Figure 5.3.: Compulsory licensing episodes by disease group based on table 2.1

From IV's point of view the likelihood of compulsory licensing differs across therapeutic areas. For potent products targeting neglected diseases (ND) the risk of encountering compulsory licensing is higher than for others. If this is anticipated by multinational pharmaceutical companies the high risk of CL inhibits investment in research and development for new drugs related to these diseases as well as costly improvements. Summarizing, diseases desperate for attention and private investment are burdened with an additional barrier to research and development investment. For a closed economy a CL heavy policy will thus have further negative impact on the treatment options of ND and should be avoided by a long term oriented government.

5.2. Generic Competitor as an Applicant

While the above model demonstrates the negotiation between innovator and government, it assumes a given duopoly outcome in case of compulsory licensing.

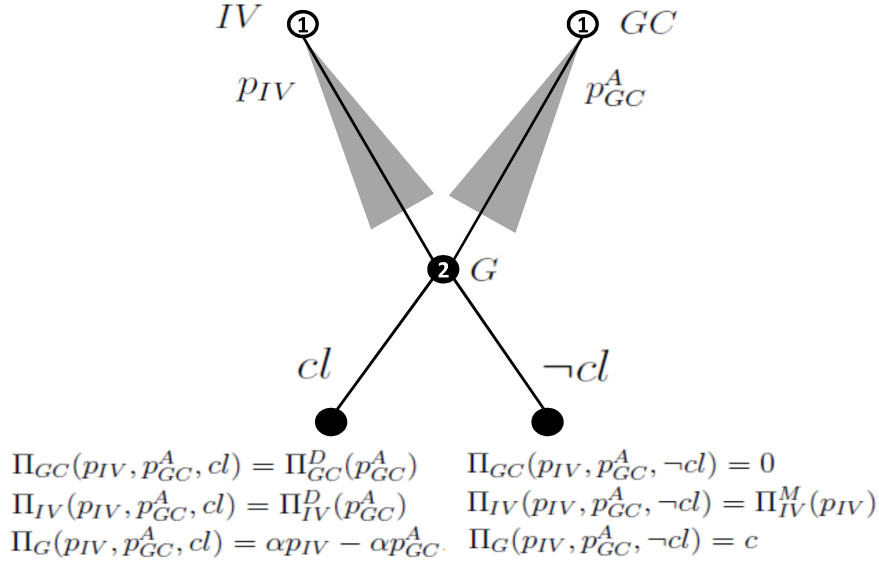


Figure 5.4.: Representation of extensive application game A

If however, the government did not commit to issue compulsory licensing a generic competitor has to apply with price p_{GC}^A and convince the government to do so. This changes the specified game N (figure 5.1) to the new game A with the extensive form depicted in figure 5.4. In game A the generic competitor submits the price p_{GC}^A simultaneously to IV proposing the negotiation price p_{IV} . It is fundamental here that while IV can change the price again for a duopoly situation, GC has to stick to p_{GC}^A so that $p_{GC}^D = p_{GC}^A$ from the above specified game N . Note that in the set of histories H_A the prices of GC and IV are denoted together and consist of the elements $\emptyset, \{p_{IV}, p_{GC}^A\}, (\{p_{IV}, p_{GC}^A\}, cl), (\{p_{IV}, p_{GC}^A\}, \neg cl)$.

The game A in extensive form is thus defined as

$$\text{set of players: } N_A = \{GC, IV, G\},$$

$$\text{set of terminal histories: } Z_A = \{(\{p_{IV}, p_{GC}^A\}, cl), (\{p_{IV}, p_{GC}^A\}, \neg cl)\},$$

$$\begin{aligned}
 &\text{player function: } \left\{ \begin{array}{l} P(\emptyset) = \{IV, GC\} \\ P(\{p_{IV}, p_{GC}^A\}) = G \end{array} \right. \quad \text{and the} \\
 &\text{preferences: } \left\{ \begin{array}{l} \Pi_{GC}(\{p_{IV}, p_{GC}^A\}, \neg cl) = 0 \\ \Pi_{GC}(\{p_{IV}, p_{GC}^A\}, cl) = \Pi_{GC}^D(p_{GC}^A) \\ \Pi_{IV}(\{p_{IV}, p_{GC}^A\}, \neg cl) = \Pi_{IV}^M(p_{IV}) \\ \Pi_{IV}(\{p_{IV}, p_{GC}^A\}, cl) = \Pi_{IV}^D(p_{GC}^A) \\ \Pi_G(\{p_{IV}, p_{GC}^A\}, \neg cl) = c \\ \Pi_G(\{p_{IV}, p_{GC}^A\}, cl) = \alpha p_{IV} - \alpha p_{GC}^A. \end{array} \right. \quad (5.4)
 \end{aligned}$$

In order to find the subgame perfect equilibrium we separate the game A into two subgames, namely $A(\emptyset)$ and $A(\{p_{IV}, p_{GC}^A\})$. Using backward induction we focus on $A(\{p_{IV}, p_{GC}^A\})$ as a first step and note that essentially not much changed from the governments perspective. As in game N and the respective subgame $N(p_{IV})$ the optimal strategy remains to issue CL only if the outcome is higher than the monopoly situation with negotiated price p_{IV} . The optimal strategy $s_G^*|_{(\{p_{IV}, p_{GC}^A\})}$ remains equivalent to 5.3 only taking into account the new application price p_{GC}^A of GC , so that

$$s_G^*|_{(\{p_{IV}, p_{GC}^A\})} = \begin{cases} cl & , \text{ for } c < \alpha p_{IV} - \alpha p_{GC}^A \\ \neg cl & , \text{ for } c \geq \alpha p_{IV} - \alpha p_{GC}^A. \end{cases} \quad (5.5)$$

The strategy $s_G^*|_{(\{p_{IV}, p_{GC}^A\})}$ is Nash equilibrium in the subgame $A(\{p_{IV}, p_{GC}^A\})$ given the prices p_{IV} and p_{GC}^A as the government cannot benefit by deviating.

Moving backwards to the first stage subgame $A(\emptyset)$ the next question is how IV

and GC will set their prices in full knowledge of the governments decision process 5.5. In particular both players have opposed preferences. While IV strives to avoid compulsory licensing, GC aims to convince G of issuing it. Essentially, the strategy for IV 5.3 remains optimal, only adjusted for the new price p_{GC}^A that IV has to deal with in a duopoly situation. It is still an optimal strategy for IV to only convince G of compulsory licensing if doing so is beneficial and thus $\Pi_{IV}^M(\frac{c}{\alpha} + p_{GC}^A) > \Pi_{IV}^D(p_{GC}^A)$. Accordingly,

$$s_{IV}^*|_{\emptyset} = \begin{cases} p_{IV} > \frac{c}{\alpha} + p_{GC}^A & \text{for } \Pi_{IV}^M(\frac{c}{\alpha} + p_{GC}^A) \leq \Pi_{IV}^D(p_{GC}^A) \\ p_{IV} = \frac{c}{\alpha} + p_{GC}^A & \text{for } \Pi_{IV}^M(\frac{c}{\alpha} + p_{GC}^A) > \Pi_{IV}^D(p_{GC}^A). \end{cases} \quad (5.6)$$

The generic competitor moves at the same time as IV and is aware of G 's decision strategy 5.5, as well. Suppose GC acts based on the following strategy. If beneficial, GC strives to achieve the opposite of IV and sets a price that will convince G to issue CL. This can be done by pricing just under the threshold of $p_{GC}^A < p_{IV} - \frac{c}{\alpha}$. This move is beneficial if undercutting the threshold of G yields a positive profit given the price needed to do this, thus $\Pi_{GC}^D(p_{IV} - \frac{c}{\alpha} - \varepsilon) > 0$. The described strategy is written as

$$s_{GC}|_{\emptyset} = \begin{cases} p_{GC}^A \geq p_{IV} - \frac{c}{\alpha} & \text{for } \Pi_{GC}^D(p_{IV} - \frac{c}{\alpha} - \varepsilon) \leq 0 \\ p_{GC}^A = p_{IV} - \frac{c}{\alpha} - \varepsilon & \text{for } \Pi_{GC}^D(p_{IV} - \frac{c}{\alpha} - \varepsilon) > 0. \end{cases}$$

with the arbitrarily small positive number ε .

Yet this strategy is not the optimal choice in all situations. Suppose that p_{GC}^{D*} is the unique optimal price which GC would set in the absence of any negotiations. Assume

further that the profit is continuously increasing in p^{GC} for $p^{GC} < p_{GC}^{D*}$ but decreasing for $p^{GC} > p_{GC}^{D*}$. If the price required to undercut the threshold is still higher than this duopoly price ($p_{IV} - \frac{c}{\alpha} - \varepsilon > p_{GC}^{D*}$) it is not optimal. GC could obtain a higher profit by pricing at p_{GC}^{D*} while still convincing G of compulsory licensing. Accordingly, the optimal strategy for GC is

$$s_{GC}^*|_{\emptyset} = \begin{cases} p_{GC}^A \geq p_{IV} - \frac{c}{\alpha} & \text{for } \Pi_{GC}^D(p_{IV} - \frac{c}{\alpha} - \varepsilon) \leq 0 \\ p_{GC}^A = p_{IV} - \frac{c}{\alpha} - \varepsilon & \text{for } \Pi_{GC}^D(p_{IV} - \frac{c}{\alpha} - \varepsilon) > 0 \\ & \text{and } p_{IV} - \frac{c}{\alpha} - \varepsilon \leq p_{GC}^{D*} \\ p_{GC}^A = p_{GC}^{D*} & \text{for } \Pi_{GC}^D(p_{IV} - \frac{c}{\alpha} - \varepsilon) > 0 \\ & \text{and } p_{IV} - \frac{c}{\alpha} - \varepsilon > p_{GC}^{D*}. \end{cases} \quad (5.7)$$

Summarizing the optimal strategies $s_{GC}^*|_{\emptyset}$, $s_{IV}^*|_{\emptyset}$ and $s_G^*|_{(\{p_{IV}, p_{GC}^A\})}$ define a subgame perfect equilibrium.

The question remains which player will come out on top and if G will issue compulsory licensing as a result. From the optimal strategies $s_{IV}^*|_{\emptyset}$ 6.1 and $s_{GC}^*|_{\emptyset}$ 5.7 we get the following conditions

$$\Pi_{IV}^M(\frac{c}{\alpha} + p_{GC}^A) > \Pi_{IV}^D(p_{GC}^A), \quad (5.8)$$

$$\Pi_{GC}^D(p_{IV} - \frac{c}{\alpha} - \varepsilon) > 0 \text{ and} \quad (5.9)$$

$$p_{IV} - \frac{c}{\alpha} - \varepsilon \leq p_{GC}^{D*}, \quad (5.10)$$

under which they are perfectly opposed. While IV aims to prevent compulsory licensing by pricing at $p_{IV} = \frac{c}{\alpha} + p_{GC}^A$, the applicant GC aims for the opposite with $p_{GC}^A = p_{IV} - \frac{c}{\alpha} - \varepsilon$. Ignore condition 5.10 for now as it demands that GC prices even

lower if unmet.

Within the boundaries of 5.8 and 5.9 no pricing equilibrium exists and figuratively speaking both competitors undercut each other's prices until one of them opts out. For a price equilibrium neither of the parties can benefit from changing their prices. Accordingly, either IV decides that decreasing the price further leads to a monopoly profit lower than for a duopoly (5.8) or GC cannot decrease the price further without suffering losses (5.9). Which equilibrium occurs depends on the costs of compulsory licensing c , the indication type α , production costs c as well as the expectations about royalty rate r .

However, we can summarize the different outcomes into three possible equilibrium categories. In one of these possibilities IV is able to lower the price p_{IV} sufficiently without GC being able to prevent G from abandoning CL efforts by pricing lower than $p_{IV} - \frac{c}{\alpha}$. Then, G refrains from compulsory licensing, IV gives a discount, GC is not able to enter the market. Intuitively, higher costs of compulsory licensing for G promote this type of outcome. Another possible equilibrium occurs if GC is able to set a price at which IV is not willing to avoid CL, just at p_{GC}^A that leads to $\Pi_{IV}^M(\frac{c}{\alpha} + p_{GC}^A) \leq \Pi_{IV}^D(p_{GC}^A)$. The third alternative appears to be pedantic, yet is essential for the upcoming analysis in chapter 6. If the optimal duopoly price p_{GC}^{D*} for GC is lower than the price necessary to defy IV , GC will choose p_{GC}^{D*} .

As a consequence, the generic price resulting from negotiations in form of the model above will always be smaller than or equal the duopoly pricing of GC without any negotiations.

5.3. Application of Discrete Asymmetric Demand

Model

The above results are mainly subject to assumptions with regard to the negotiating game model and only few relate to any characteristics of demand, specifically the duopoly situation. The following will implement the discrete asymmetric duopoly model introduced in chapter 3 within the negotiation game in order to visualize the results and clarify. Most notably, while the upcoming application imposes further assumptions the general results from above are taken forward to the next chapter 6.

For the discrete asymmetric duopoly model we can express the profit functions of IV (3.16) and GC (3.17) in case of CL as

$$\begin{aligned}\tilde{\Pi}_{IV}(\tilde{p}_{IV}, \tilde{p}_{GC}) &= (1 - \tilde{\alpha})(1 + \tilde{p}_{GC} - \tilde{p}_{IV})(\tilde{p}_{IV} - vc) \\ &\quad + (1 - \tilde{\alpha})r\tilde{p}_{GC}(\tilde{p}_{IV} - \tilde{p}_{GC}) + \tilde{\alpha}r\tilde{p}_{GC} \text{ and} \\ \tilde{\Pi}_{GC}(\tilde{p}_{IV}, \tilde{p}_{GC}) &= (1 - \tilde{\alpha})(\tilde{p}_{IV} - \tilde{p}_{GC})((1 - r)\tilde{p}_{GC} - vc) \\ &\quad + \tilde{\alpha}((1 - r)\tilde{p}_{GC} - vc)\end{aligned}$$

by using the urban demand functions 3.3, 3.2 and assuming full coverage of rural area in case of CL. While GC applies for CL with p_{GC}^A and is required to retain it, IV can set a new price. This optimal pricing of IV as a response to GC pricing p_{GC}^A is

$$\begin{aligned}\tilde{\Pi}_{IV} &= (1 - \tilde{\alpha})(1 + \tilde{p}_{GC} - \tilde{p}_{IV})(\tilde{p}_{IV} - vc) \\ &\quad + (1 - \tilde{\alpha})r\tilde{p}_{GC}(\tilde{p}_{IV} - \tilde{p}_{GC}) + \tilde{\alpha}r\tilde{p}_{GC} \\ \Rightarrow 0 &= (1 - \tilde{\alpha})(1 + (1 + r)\tilde{p}_{GC} + vc - 2\tilde{p}_{IV})\end{aligned}$$

$$\Rightarrow \tilde{p}_{IV}^D(\tilde{p}_{GC}) = \frac{1 + vc + (1 + r)\tilde{p}_{GC}}{2}.$$

This result is similar to 3.18 in which $\alpha = 0$ was assumed, because IV does not have influence on rural area demand. Inserting the optimal response price \tilde{p}_{IV}^D in the profit functions of IV and GC results in long terms which are expressed as $\tilde{\Pi}_{IV}^D(\tilde{p}_{GC}^A)$ and $\tilde{\Pi}_{GC}^D(\tilde{p}_{GC}^A)$ henceforth. Here, \tilde{p}_{GC}^A is GC 's application price and not the optimal duopoly price. Summarizing, the preferences of game A change and the new game \tilde{A} is defined as:

$$\begin{aligned} \text{set of players: } N_{\tilde{A}} &= \{GC, IV, G\}, \\ \text{set of terminal histories: } Z_{\tilde{A}} &= \{(\{p_{IV}, p_{GC}^A\}, cl), (\{p_{IV}, p_{GC}^A\}, \neg cl)\}, \\ \text{player function: } &\begin{cases} P(\emptyset) = IV, GC \\ P(\{p_{IV}, p_{GC}^A\}) = G \end{cases} \quad \text{and the} \\ \text{preferences: } &\begin{cases} \Pi_{GC}(\{p_{IV}, p_{GC}^A\}, \neg cl) = 0 \\ \Pi_{GC}(\{p_{IV}, p_{GC}^A\}, cl) = \tilde{\Pi}_{GC}^D(\tilde{p}_{GC}^A) \\ \Pi_{IV}(\{p_{IV}, p_{GC}^A\}, \neg cl) = (1 - \alpha)(p_{IV} - vc) \\ \Pi_{IV}(\{p_{IV}, p_{GC}^A\}, cl) = \tilde{\Pi}_{IV}^D(\tilde{p}_{GC}^A) \\ \Pi_G(\{p_{IV}, p_{GC}^A\}, \neg cl) = c \\ \Pi_G(\{p_{IV}, p_{GC}^A\}, cl) = \alpha\tilde{p}_{IV} - \alpha\tilde{p}_{GC}^A. \end{cases} \quad (5.11) \end{aligned}$$

Figures 5.5 and 5.6 show the profit of GC if compulsory licensing is issued ($\tilde{\Pi}_{GC}^D(\tilde{p}_{GC}^A)$) in dependence of the application price \tilde{p}_{GC}^A . Further, the figures show IV 's profit in the case of duopoly ($\tilde{\Pi}_{IV}^D(\tilde{p}_{GC}^A)$) and monopoly ($\tilde{\Pi}_{IV}^M(\frac{c}{\alpha} + \tilde{p}_{GC}^A)$). The latter can be displayed in dependence of p_{GC}^A as well, when undercutting $p_{IV} = \frac{c}{\alpha} + \tilde{p}_{GC}^A$ so that

G refrains from issuing compulsory licensing.

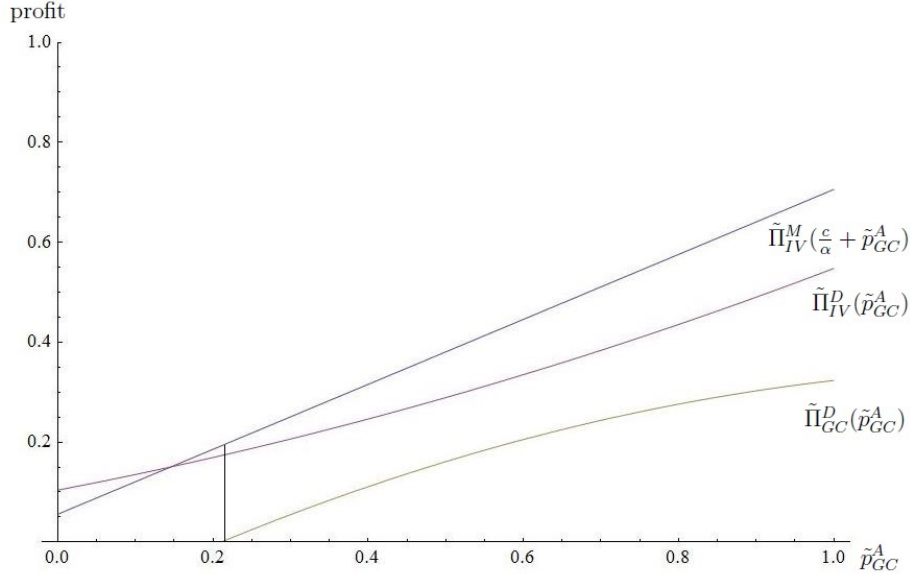


Figure 5.5.: Example of game \tilde{A} with outcome no CL: Profit functions of GC and IV in dependence of p_{GC}^A for parameters $C = 0.1$, $vc = 0.2$, $r = 0.05$ and $\alpha = 0.35$

While the curves in figure 5.5 are given for the exemplary values of $C = 0.1$, $vc = 0.2$, $r = 0.05$ and $\alpha = 0.35$, figure 5.5 only differs in terms of $\alpha = 0.5$. In the scenario of figure 5.5 ($\alpha = 0.35$) the innovator IV is able to benefit from undercutting even the lowest prices \tilde{p}_{GC}^A that GC would set with positive non negative profit. Consider $\tilde{p}_{GC}^A \approx 0.21$ which results in zero profit for GC : Here IV is still able to achieve more profit from undercutting this price with $\tilde{p}_{IV} = \frac{c}{\alpha} + \tilde{p}_{GC}^A$ than by accepting compulsory licensing. As a result IV proposes just this price which makes it impossible for GC to successfully convince GC of CL while still achieving profit, G accepts and refrains from issuing CL. In figure 5.5 on the other hand, we are looking at a therapeutic area more directed towards the poor population in rural areas and thus with a higher $\alpha = 0.5$. In this case the G will issue CL since GC is able to price at a level for which IV refrains from undercutting. This demonstrates that for higher α compulsory licensing becomes more likely. Increasing the costs C of compulsory licensing for G on the other hand decreases the probability of CL by shifting $\tilde{\Pi}_{IV}^M(\frac{c}{\alpha} + \tilde{p}_{GC}^A)$ sideways

and making it easier for IV to undercut with $p_{IV} = \frac{c}{\alpha} + \tilde{p}_{GC}^A$.

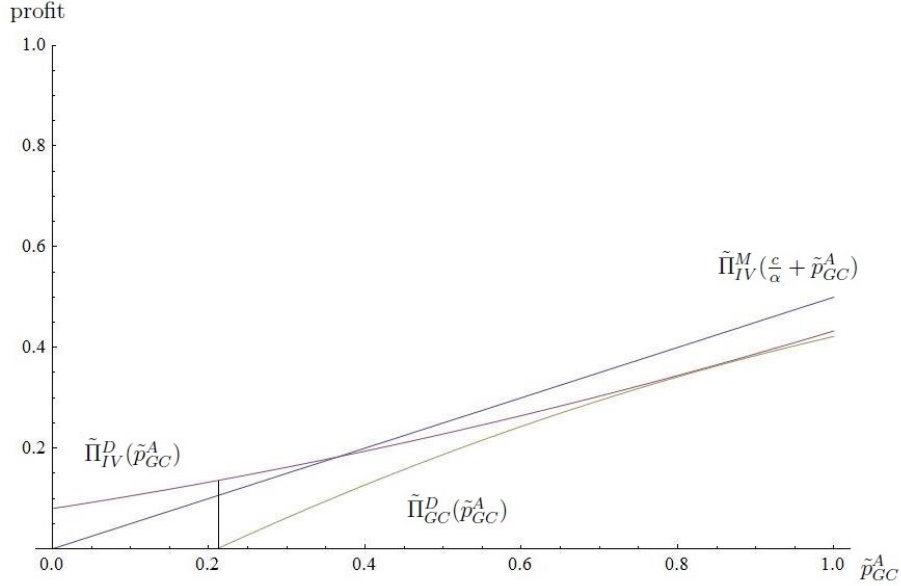


Figure 5.6.: Example of game \tilde{A} with outcome CL: Profit functions of GC and IV in dependence of p_{GC}^A for parameters $C = 0.1$, $vc = 0.2$, $r = 0.05$ and $\alpha = 0.5$

5.4. Conclusion

After having discussed static compulsory licensing duopoly pricing in chapter 3 we pursued the question which effect negotiations have in this chapter. As a first step we depict a dynamic negotiation game with perfect information in extensive form and model the widely observed discounts resulting from CL negotiations. In a second step this game is extended to account for the fact that potential licensees apply for CL with their price. As a result the licensee's price could be lower compared to the profit maximizing duopoly choice. This is an important finding because it shows that negotiations with both, innovator as well as private generic manufacturer are the key element for governments to ensure access via low generic prices.

These findings are fully supported by the well documented case of compulsory licensing in India for the drug Nexavar in March 2012. It shows that the domestic

generic competitor Natco Pharma Limited applied for CL with a low price to convince the government of CL. As detailed in the decision (Government of India (2012)) this price and the estimated access to the drug compared to Bayer's pricing was the main driver for the positive decision. What makes this decision unique in the context of our analysis is that prior to the CL, Cipla Limited, another domestic manufacturer effectively already created a duopoly by selling a counterfeit, unauthorized drug. The converted price of \$ 600 monthly for this drug apparently marks the optimal duopoly price from Cipla's point of view, given the structure of demand and Bayer's price of \$ 5,600 monthly. While \$ 600 is the price of choice without negotiations, Natco applied with a price of \$ 180 per month for CL. We cannot assess if this price is driven by application considerations, competitive pricing versus Cipla or a composition of both. However, note that Natco fixed this price while being fully aware of Bayer's filed infringement suit against Cipla.

Summarizing, there is space for domestic generic manufacturers to decrease the price for a CL application compared to the profit maximizing duopoly price, if necessary. Companies will do so in order to convince a government of compulsory licensing. One could argue that the government's preferences might not be common knowledge and in particular the costs of compulsory licensing are unknown. However, in this case price reductions influence the likelihood of compulsory licensing from the generic's point of view.

Note that negotiations with a domestic generic manufacturer are unnecessary for government owned manufacturers as it was the case for CL episodes in Brazil. Further, the application concept only holds if the respective government did not commit to compulsory licensing prior to negotiations. This case will be at the center of discussion when we relax the restriction of a closed economy in the next chapter.

6. Open Economy

The foregoing analysis looked at the compulsory licensing instrument from different angles and in each chapter we focus on a single mechanic by fading out others. In this chapter all findings and mechanisms are brought together to form a big picture.

The compulsory licensing instrument concedes members of the World Trade Organization a derogation to harmonized patent protection. In individual cases countries are allowed to compulsory license (CL) a generic manufacturer with the production and marketing of a patented product. In this case a duopoly is established in which the innovator's (IV) product is perceived as superior in quality and the domestic generic competitor (GC) benefits from an extensive distribution network. Accordingly, we conclude from chapter 3 that the competition is not perfect and prices remain above marginal costs. Further, the royalty increases in the licensee's price depending on the marginal costs and the degree of competition. Yet, chapter 5 depicts that the generic manufacturer applies for compulsory licensing and pricing is driven by the goal to persuade compulsory licensing rather than the static duopoly situation. This finding does only hold if the country did not commit to compulsory licensing prior to price negotiations. Additionally, compulsory licensing usage could lead to reduced incentives for research in affected therapeutic areas such as neglected diseases due to anticipation of investors in a closed economy.

In this chapter we ask how these findings turn out when we dispense with the restriction of a closed economy. Furthermore selected alternatives and enhancements are discussed and compared in light of the identified problems.

6.1. Free Riding, Differential Pricing and Parallel

Imports

One of the results from the foregoing chapter 5 is that CL is more likely to be issued for drugs targeting neglected diseases (ND) and communicable diseases than for others. This impacts the expected return of research and development projects in such therapeutic areas and adds to the already reduced efforts due to the low out of pocket purchasing power of the affected poor population. From a closed economy perspective a CL heavy strategy on these diseases is not welfare efficient in the long run as it probably reduces the treatment options.

Relaxing the restriction of closed economy and roughly segmenting the world into developed and developing nations does revise this trade off between long term and short term considerations. For global diseases the required profits to motivate research and development (R&D) can usually be made in developed countries alone and the return from selling drugs in developing countries plays a minor role in an investment decision. For ND the situation is reversed but profits from developing countries do not motivate large R&D investments. Extensive CL usage for NDs will diminish even these investment incentives and reduce treatment options in the long run. Thus, for developing countries as one entity CL might possibly not lead to higher welfare in the long run and other methods of providing access should be applied. Yet, a classic free rider dilemma arises and an individual sufficiently small

developing country might benefit from stepping out of line and pursue a CL policy for NDs.

A contractual commitment to refrain from CL usage for specific therapeutic areas would reduce risks of investment and increase private R&D for NDs. In order to improve access and ensure funding an option is to reimburse patented drugs for ND while applying CL on medications targeting global diseases. If developing countries contribute to improve the return of pharmaceutical R&D investment it should be for neglected domestic diseases, rather than for global diseases. At this point the advanced market commitment (AMC) mechanism introduced in section 4.2.3 gains additional importance. Donator countries or even LDC themselves commit to purchase novel drugs that achieve a predefined target product profile for neglected diseases. This way the anticipated likely compulsory licensing policy would be recovered by reliable contractual commitments. The AMC mechanism is designed to correct free-rider dilemma and the time inconsistencies which hinder innovation by anticipated ex post price pressure and compulsory licensing for neglected diseases. While publications by Kremer and Glennerster (2004) or Berndt et al. (2007) do not consider that compulsory licensing is more likely for neglected diseases this analysis strengthens their argumentation and emphasizes the need for further deployment of the AMC tool.

With regard to access, a segmentation of target countries and differential pricing is feasible and could even be maximizing the return of investment (World Health Organization (2001), p. 3.) for innovators. Hence, prices in developing countries should be significantly lower than prices in developed countries. Yet, there are serious obstacles that prohibit global pharmaceutical companies from conducting efficient differential pricing even though it would most probably increase total welfare.

Some countries use a so called "reference price system" when setting upper price limits or reimbursement policies. This means, for instance, that a government using such a system will not reimburse a certain drug if the price is higher than in another country. Hence pharmaceutical companies might decide to price higher in relatively small markets in order to push up the price for the drug in the major markets. This effect is not only restricted to implemented systems but additionally impacts price negotiations in general. For example consider the Brazil price negotiations in the context of CL for Efavirenz as detailed in section 2.2. The CL was issued because the innovator MSD did not lower its price for the drug to the same level as it did after the CL negotiations in Thailand. Summarizing, a relatively low price in one country potentially influences the reimbursed price in other countries, which deters differential pricing.

Another factor that hinders differential pricing are so called parallel imports, also referred to as gray trade. While patents concede the right to exclude others from selling a product to the patent holder this right is exhausted upon initial sale within the country (A). As a result the patent holder loses control over the product and it can be redistributed by the new possessor in A. The question if this product can be sold in another country (B) depends on B's legislation and exhaustion regime. In case of national exhaustion the right to exclude others is only exhausted on a national level, not applying to the country B. Accordingly, the possessor cannot resell the product in B without the right holder's approval. If B uses a system of international exhaustion it considers the right to exclude others as exhausted internationally and allows the import for sale. Note that parallel trade is possible to B regardless of the exhaustion system in A. As an example members of the European Union apply a doctrine of international exhaustion with regard to other member countries, yet national exhaustion is applied for countries outside of EU. Parallel trade from country

A to country B could force the prices in B down if the innovator of a drug does not bind its manufacturers in A to relatively equivalent prices (Tirole (2006)). Innovators anticipating parallel trade might decide to refrain from differential pricing and protect sales in high income countries.

While the above described factors of reference pricing systems and parallel trade inhibit price differential pricing they potentially also hinder price negotiations related to compulsory licensing. Suppose these concerns from an innovator's point of view can be expressed as a function $G(p_{IV})$ of the negotiated price. Then, the preferences 5.4 from game A depicted in section 5.2 become

$$\Pi_{IV}(\{p_{IV}, p_{GC}^A\}, \neg cl) = \Pi_{IV}^M(p_{IV}) - G(p_{IV}).$$

Consequentially, the strategy $s_{IV}^*|_{\emptyset}$ needs to be adjusted to

$$s_{IV}^*|_{\emptyset} = \begin{cases} p_{IV} > \frac{c}{\alpha} + p_{GC}^A & \text{for } \Pi_{IV}^M(\frac{c}{\alpha} + p_{GC}^A) - G(\frac{c}{\alpha} + p_{GC}^A) \leq \Pi_{IV}^D(p_{GC}^A) \\ p_{IV} = \frac{c}{\alpha} + p_{GC}^A & \text{for } \Pi_{IV}^M(\frac{c}{\alpha} + p_{GC}^A) - G(\frac{c}{\alpha} + p_{GC}^A) > \Pi_{IV}^D(p_{GC}^A), \end{cases} \quad (6.1)$$

in order to be subgame perfect. This means that government and innovator are less likely to come to an agreement. Additionally, the generic competitor's application price p_{GC}^A increases. Importantly, the relation of $\Pi_{IV}^M(p_{IV})$ within the country and costs of price reduction outside the country $-G(p_{IV})$ is less favorable for LDC.

6.2. Cross Border Compulsory Licensing

Before the Doha declaration in 2001 the WTO permitted compulsory licensing for domestic use only. Hence, least developed countries (LDC) without the infrastructure

to produce drugs with sufficient quality were not able to benefit from the compulsory licensing provision.¹ If the drug was under patent for all other countries, there would be no possibility to import the drug even though the LDC issued compulsory licensing. This changed when in 2001 the WTO ministerial conference in Doha allowed compulsory licensing for export. Cross border compulsory licensing (CBCL) became possible if both countries, the exporting nation as well as the importing LDC, issue compulsory licensing. Yet, CBCL was used only once when the Canadian generic manufacturer Apotex exported the antiretroviral triple combination Zidovudine, Lamivudine and Nevirapine to Rwanda in 2008. From the documentation of this case, amongst others by Apotex (2008), Weber and Mills (2010) or Kyle and McGahan (2011), we know that the process was very cumbersome. Yet, complexity in the application or a time consuming process as detailed in section 2.3 should not prevent countries of CBCL, especially if supported by organizations such as Médecins Sans Frontières (MSF) or the Clinton Foundation.

Two important issues stand out even though both apply for any country which considers compulsory licensing, capable of domestic production or not. First of all there are barriers to compulsory licensing in form of pressure from innovators, investors or countries. However, this did not prevent multiple other compulsory licenses so the question remains why CBCL usage should be prevented. Secondly, Apotex (2008) and Weber and Mills (2010) report that countries are reluctant to self-identify at an early stage of the cross border compulsory licensing process. Again, all countries that issue compulsory licensing self-identify eventually, which is the point when the costs of pressure from innovators or governments trigger. It remains unclear why exactly LDC are unlikely to utilize CBCL while generally compulsory licensing is frequently used.

¹The abbreviation LDC used henceforth refers to these countries

Recall that India does not register patents for drugs introduced before 2005 and thus can export older products without CL. A number of LDC issued CL for drugs not under patent in India and imported them. Let us call such import compulsory licensing (ICL) in contrast to domestic compulsory licensing (DCL) with domestic production. This is not CBCL as refereed to by the Doha declaration as it requires two compulsory licenses.

The upcoming will depict two concrete disadvantages that CBCL has over DCL as well as ICL. We show that the incentive to issue CBCL is inferior to the incentive for DCL or ICL. Firstly, the focus lies on the static duopoly already discussed in chapter 3 and transportation costs, which occur for CBCL as well as ICL. These costs do not only add to the marginal cost of the licensee's product but additionally increase the cost amplified effect of royalty on price. For ICL and DCL however, the generic optimal duopoly price is overwritten by the application price a generic manufacturer bids to convince a government of compulsory licensing. A LDC has to self identify at an early stage of a cumbersome and time consuming CBCL process and thus commit to compulsory licensing prior to negotiations. Still, a potential licensee has to convince the LDC of CL, but not under consideration of barriers. These barriers are already teared down by the LDC by engaging in CL negotiations in the first place and persuading CL. Hence, the costs of CL can be regarded as sunk costs in a negotiation process.

6.2.1. Royalty and Cross Border Compulsory Licensing

The WTO TRIPs agreement regulates that the generic licensee is obligated to transfer a remuneration to the innovator if compulsory licensing is issued. Height and character of this remuneration is determined by the respective national government.

As discussed in chapter 3.3, these remunerations are almost exclusively low royalties based on net generic sales.

Following the Doha declaration these remunerations are payed for by the exporting firm in case of CBCL (World Trade Organization (2003)). Additionally, the export of goods is usually costly in terms of transportation costs. Suppose transportation t costs can be broken down to single units and increase in the number. In accordance with 3.9 the exporting licensee's objective function hence becomes

$$\Pi_{GC} = D_{GC}(p_{GC}, p_{IV})((1 - r)p_{GC} - vc - t), \quad (6.2)$$

with IV 's price p_{IV} , GC 's price p_{IV} alias the licensee, transportation and variable costs $vc + t$ and royalty r per sales. We assume here that the product in the target country is either distributed by the same exporting company or by the government without price increase. Profit maximization leads to the optimal price

$$\begin{aligned} p_{GC}^* &= \frac{D_{GC}(p_{GC}, p_{IV})}{-\frac{\partial D_{GC}(p_{GC}, p_{IV})}{\partial p_{GC}}} + \frac{vc + t}{1 - r}, \text{ or} \\ \Leftrightarrow p_{GC}^* &= \frac{D_{GC}(p_{GC}, p_{IV})}{-\frac{\partial D_{GC}(p_{GC}, p_{IV})}{\partial p_{GC}}} + vc + t + (vc + t)\frac{r}{1 - r}, \end{aligned} \quad (6.3)$$

with the royalty amplification effect $t\frac{r}{1-r}$ as well as the direct effect of t on the price p_{GC}^* . Summarizing, the effect of the royalty on the generic price is higher than expected. As discussed in chapter 5 the duopoly optimal price and hence these effects could be overwritten by negotiations.

6.2.2. Negotiations and Cross Border Compulsory Licensing

For DCL as well as ICL the generic competitor approaches the government and automatically triggers a predefined process, while the outcome is open. The respective compulsory licensing episode could close with a discount, voluntary licensing, compulsory licensing or no action. Generic manufacturer (GC) and innovator (IV) negotiate with the government (G) simultaneously. Ultimately G comes to a decision based on the proposed prices p_{IV}, p_{GC}^A and the costs of compulsory licensing c . As demonstrated in the extensive game A with perfect information this could lead to reduced pricing. In particular the applicant GC aims to convince G of issuing CL with a low price p_{GC}^A while IV counters in a bargaining downward spiral.

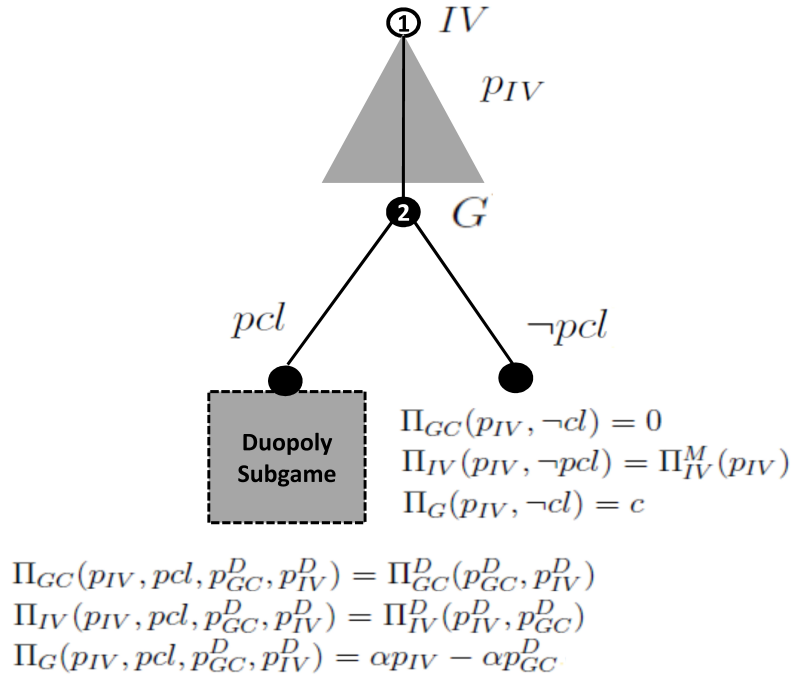


Figure 6.1.: Representation of extensive commitment game C

For CBCL the sequence of moves differs and an importing country self-identifies at an early stage (Apotex (2008) or Weber and Mills (2010)). By reaching out to foreign

exporters the respective country shows the world that it is willing to issue compulsory licensing and effectively annul intellectual property rights. If CL is not issued in the end it is not because the respective LDC refrains from doing so. The only question which remains is if a suitable generic manufacturer can be found capable of exporting from a country willing to issue a CL as well.

Consider the extensive form game C represented in figure 6.1. Essentially the game C is similar to the game A but with the generic competitor GC included. In the game C we look at the three players innovator (IV), government (G) and generic competitor (GC). As a start IV sets the price p_{IV} on which G reacts with the decision to reach out and pursue CL pcl or not $\neg pcl$. We assume here that if G decides to pursue compulsory licensing a generic competitor will be found from a country willing to issue compulsory licensing for this purpose. This assumption is not problematic since many WTO members have a legislation in place similar to the Canadian "Access to Medicines" Regime, for example in the EU or USA (Government of Canada (2006) Annex B). If G decides to accept IV 'S price no CL is issued and the game ends. IV 's profit in that case is defined as $\Pi_{IV}^M(p_{IV})$ in dependence of the price p_{IV} priorly offered. By declaring the negotiations with IV as collapsed and pursuing CL the respective LDC triggers the costs $-c$ of CL. At this point a duopoly subgame unfolds which does not need to be detailed for the purpose of this analysis. The outcomes are given by IV 's profit $\Pi_{IV}^D(p_{IV}^D, p_{GC}^D)$, GC 's profit $\Pi_{GC}^D(p_{GC}^D, p_{IV}^D)$ and G preferences $\alpha p_{IV} - \alpha p_{GC}^D$.

Summarizing, the game C in extensive form is defined as

$$\text{set of players: } N_C = \{IV, G, GC\},$$

$$\text{set of terminal histories: } Z_C = \{(p_{IV}, pcl, p_{GC}^D, p_{IV}^D), (p_{IV}, \neg pcl, p_{GC}^D, p_{IV}^D)\},$$

$$\begin{array}{lcl}
 \text{player function:} & \left\{ \begin{array}{l} P(\emptyset) = IV \\ P(p_{IV}) = G \\ P(p_{IV}, p_{cl}) = \{GC, IV\} \end{array} \right. & \text{and the} \\
 \text{preferences:} & \left\{ \begin{array}{l} \Pi_{IV}(p_{IV}, \neg p_{cl}) = \Pi_{IV}^M(p_{IV}) \\ \Pi_{IV}(p_{IV}, p_{cl}, p_{GC}^D, p_{IV}^D) = \Pi_{IV}^D(p_{IV}^D, p_{GC}^D) \\ \Pi_{GC}(p_{IV}, \neg cl) = 0 \\ \Pi_{GC}(p_{IV}, p_{cl}, p_{GC}^D, p_{IV}^D) = \Pi_{GC}^D(p_{GC}^D, p_{IV}^D) \\ \Pi_G(p_{IV}, \neg cl) = c \\ \Pi_G(p_{IV}, p_{cl}, p_{GC}^D, p_{IV}^D) = \alpha p_{IV} - \alpha p_{GC}^D. \end{array} \right. & (6.4)
 \end{array}$$

To exclude empty threads as well as empty promises we look at subgame perfect equilibria and use backward induction. This means that the outcome of the duopoly is derived within this very subgame only. Without going into detail with the duopoly situation we assume subgame perfect strategies for both players IV and GC

$$\begin{aligned}
 s_{IV}^*|_{p_{IV}, p_{cl}} &= p_{IV}^{D*}(p_{GC}^D) \\
 s_{GC}^*|_{p_{IV}, p_{cl}} &= p_{GC}^{D*}(p_{IV}^D).
 \end{aligned}$$

We write the equilibrium prices as p_{IV}^{D*} and p_{IV}^{D*} . Note here, that GC does not take into account any considerations of G . GC sets the optimal price given the duopoly demand situation, royalties as well as IV 's price p_{IV}^D . These optimal prices p_{IV}^{D*} and p_{IV}^{D*} denote a subgame perfect equilibrium as neither GC nor IV can benefit from deviation. The resulting price accordingly is always higher or equals the application price p_{IV}^A .

Yet, stepping back one stage to the subgame $C(p_{IV})$ the government G anticipates this price and decides about compulsory licensing. This decision is based on the subgame perfect equilibrium price p_{IV}^{D*} and the proposed monopoly price p_{IV} resulting from the first stage of game C . Similar to game N and A it remains G 's optimal strategy to issue CL only if it the outcome is higher than for the monopoly situation, taking into account the costs. Accordingly, the strategy

$$s_G^*|_{p_{IV}} = \begin{cases} pcl & , \text{ for } c < \alpha p_{IV} - \alpha p_{GC}^{D*} \\ \neg pcl & , \text{ for } c \geq \alpha p_{IV} - \alpha p_{GC}^{D*} \end{cases} \quad (6.5)$$

gives G 's subgame perfect equilibrium strategy.

Moving further backwards leads us to the subgame $C(\emptyset)$ in which IV proposes the monopoly price. IV anticipates G 's strategy and sets p_{IV} in accordance. For a strategy to be subgame perfect IV will use a lowered price p_{IV} to prevent CL only as long as this is profitable so that $\Pi_{IV}^M(p_{IV}) > \Pi_{IV}^D$. In order to do that IV will price just under the threshold $p_{IV} = \frac{c}{\alpha} + p_{GC}^{D*}$. Summarizing IV 's strategy

$$s_{IV}^*|_{\emptyset} = \begin{cases} p_{IV} > \frac{c}{\alpha} + p_{GC}^D & \text{for } \Pi_{IV}^M(p_{IV}) \leq \Pi_{IV}^{D*} \\ p_{IV} = \frac{c}{\alpha} + p_{GC}^D & \text{for } \Pi_{IV}^M(p_{IV}) > \Pi_{IV}^{D*}, \end{cases} \quad (6.6)$$

is a subgame perfect equilibrium. IV cannot benefit by deviating from $s_{IV}^*|_{\emptyset}$ within this subgame.

Compared to the application game A we see that CBCL is at a disadvantage. For A this price either equals or is lower than in this setting C . The reason lies within the early identification and decision to pursue CL. GC does not need to apply for compulsory licensing and takes the decision as given.

6.3. Conclusion

The previous chapters dealt with isolated aspects of compulsory licensing (CL) such as the duopoly pricing rational (3), incentives for research (4) or the aspect of negotiations (5). In this chapter we bring the findings from these chapters together and examine them against the background of an open economy.

Chapter 5 showed that CL is more likely to be issued for diseases predominantly affecting the poor while at the same time we know that in particular these diseases are lacking private investment in research and development (R&D). Not only might government's preferences be time-inconsistent *id est* encouraging innovation prior to and striving for cost effective access after the invention in a closed economy. Additionally, developing nations all together face a free-rider dilemma in encouraging investments in particular regarding the usage of CL. The advanced market commitment (AMC) mechanism introduced in chapter 4 could be one solution to approach this dilemma for specific diseases. Further, we describe how differential pricing is hampered by reference price systems as well as parallel trade. In the same way these two topics influence the innovator's willingness to price discriminate between countries, both discourage innovators to slash prices during CL negotiations. The costs to an innovator induced by discounts based on parallel trade and reference price systems become relatively high compared to the market value of least developed countries (LDC). Accordingly LDCs are at a disadvantage negotiating with innovators about discounts prior to CL.

Compulsory licensing in the context of open economy is either domestic CL (DCL), import CL (ICL) or cross border compulsory licensing (CBCL). For CBCL both, the importer and the exporter are required to issue CL. For ICL as well as CBCL transportation costs would add to the production costs of a drug. These impact

the optimal price from the generic manufacturer's point of view directly as well as indirectly by means of a royalty based on sales.

From chapter 5 we know that this optimal price could be overwritten by the generic manufacturer applying for CL with an application price. For CBCL however, the sequence of moves in the negotiation game differs and the generic competitor does not apply for CL. LDCs intending to issue CL have to self identify at an early stage and trigger the costs of compulsory licensing prior to negotiations with a generic competitor. This means that negotiations with IV and GC are not taking place at the same time and more importantly the government commits to CL. A generic competitor will thus set the optimal duopoly price and is not tempted to grand discounts to convince the government of CL in the first place. LDCs anticipate this behavior and as a result could decide to refrain from CL even though it would be beneficial to do so from the government's as well as the generic competitor's point of view.

Summarizing, LDCs are subject to several discriminations with regard to compulsory licensing. First, LDCs are not able to benefit from negotiation with generic manufacturers as they commit to CL before these take place. Second, the optimal price a generic manufacturer would choose is higher than compared to domestic production. Transportation costs directly add to the optimal duopoly price while additionally a royalty based on sales amplifies this effect. Third, the innovator's willingness to grant discounts during negotiations prior to CL is hampered. LDCs offer relative low revenue savings compared to the global costs in terms of parallel trade and reference price systems.

7. Summary, critique and further research

The work at hand presents one main finding which derives from a combination of multiple results throughout the analysis. Least developed countries (LDC) not capable of appropriate domestic drug production are not able to fully benefit from compulsory licenses (CL) because they are unintentionally discriminated compared to countries with domestic production capabilities. This discrimination is hidden within the mechanics induced by the instrument. While cross border compulsory licensing (CBCL) is allowed under the World Trade Organization's regime of "Trips Related Aspects of Intellectual Property Rights", the barriers to CL identified in the literature to date lack any specifics regarding LDCs.

The reason for the discrimination is that governments (G) striving for CBCL have to self identify at an early stage and reach out to generic manufacturers in other countries. Between the negotiations with a patent holder, self identification, first negotiations with a generic manufacturer, CLs in both exporting and importing country and a final contract lies a long and cumbersome registration process. Yet, for domestic compulsory licensing (DCL) a generic competitor (GC) takes the initiative and files a request for CL. Not only does this give G an opportunity to fully assess the

implications before self identifying. Additionally, this sequence forces GC to apply with a tempting price. Countries with government owned generic manufacturers are also able to assess the situation without self identifying early and achieve generic prices at marginal costs.

These differences between DCL and CBCL would not lead to a discrimination if it was not for the following two factors making the negotiations prior to a CL crucial.

Firstly, the competition that unfolds after a CL is not perfect. Because of the innovator's (IV) quality advantage and a wider distribution network of GC the generic price will not be at marginal costs level. Additionally, a remuneration by net sales does further increase the generic optimal duopoly price. This effect is amplified by the production costs and increased for CBCL by transportation costs. The optimal duopoly price however is annulled by negotiations prior to DCL. For CBCL, G commits to CL prior to negotiations with GC and as a result the higher generic optimal duopoly price applies.

Secondly, there are costs of CL which the respective government has to consider. These costs include negative factors such as pressure from other nations and a potential reduction of foreign direct investment due to perceived weakened intellectual property protection. In order to convince the government of CL a generic competitor thus has to further decrease the price and undercut the discounted innovator's offer as well as the costs of compulsory licensing. For LDC requiring CBCL these costs are triggered when self identifying at an early stage and rejecting IVs discount offer.

Summarizing, LDCs might refrain from CL even though it would be beneficial for both, G as well as the GC to have a CL in place. It is only due to the sequence of moves that GC decides to price at optimal duopoly competition level if CL is issued. Importantly, any other strategy is an empty promise. This price, however,

is anticipated by G and might not be sufficient to issue CL in the first place, given the costs of CL.

In order to encourage foreign generic manufacturers to reach out to LDC and apply for compulsory licensing the export CL needs to be automatic rather than intransparent, time consuming and cumbersome. This is important not to reduce the duration of the process per se, but to give the LDC a better position in negotiations and encourage generic manufacturers to reach out. Another option is for LDCs to consider multiple compulsory licenses *ab initio* and assume marginal cost pricing as a result from several GCs. This, however, is feasible only for least developed countries with multiple domestic distributors.

A topic to consider in further research is the relation between domestic distributor and exporting manufacturer, since in this analysis we assumed the distributor to be a mere distribution extension of the exporter. Also, for the line of arguments presented here the specifics of the duopoly resulting from CL are negligible. Nonetheless, further research on the compulsory licensing duopoly could test the two dimensional demand model and narrow down characteristics. This would be beneficial in particular with regard to neglected diseases as well as voluntary licensing and monopoly profits. Apart from other reasons this topic is complex and interesting due to pharmacovigilance hurdles. In addition, we assume the costs of compulsory licensing to be public knowledge in order to simplify the analysis. Yet, it might be more accurate to understand the costs as an unknown of which IV and GC form expectations. Auxiliary, an issued CL could be interpreted as a signal influencing the expectations of other investors and denoting the costs of CL, in terms of hampered foreign direct investment.

Another result is that compulsory licensing is in particular likely for diseases pre-

dominantly affecting the poor population, neglected diseases. If a CL is issued the induced competition will improve access due to low price generics. The government's decision is assumed to be driven by cost savings under full supply, mirroring this access width. This might lead to the inappropriate situation in which developing countries avoid CL for global diseases and issue CL for neglected diseases. Yet, from the perspective of developing countries as a united entity it would be more beneficial to allocate resources just the other way around, to free-ride on global disease research and to encourage investment in neglected diseases. As a solution, so called Advanced Market Commitments could be used to assure time consistent incentives.

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A. Appendix

A.1. Details on Compulsory Licensing Assessment

Table 2.1 chronologically details a collection of compulsory licensing episodes based on Beall and Kuhn (2012b). It is non-exclusive since generally, CL is not obligatory to WTO notifications. To qualify for the list the respective government has to show support and a mere application for CL or threat from a generic manufacturer does not suffice. Further the involved country has to be a WTO member for the CL to be listed. Accordingly, CL episodes from Cameroon and Eritrea are not taken into consideration. The differences to Beall and Kuhn (2012b) are as follows:

1. Additional information on royalty rates, affected molecule and corporation as well as the generic manufacturer have been added, if reliable sources are available. These numerous sources are given in the columns S1-S4 via characters assigned to a source in the tables description.
2. Table 2.1 gives each affected molecule separately, whereas Beall and Kuhn (2012b) display episodes. Thereby, the impact of episodes that affect several corporations can be assessed at a glance. The only exception are the CL episodes in Zimbabwe and Ghana (rows 4 & 26, respectively) which issued CLs on all medications related to HIV and thus are difficult to assess.

3. In order to focus on developing countries only, CL episodes in high income countries are not considered.
4. Five episodes have been added to the list:
 - a) One new CL which was issued in the first quarter of 2012 by India (row 43) after Beall and Kuhn (2012b) was published (Government of India (2012)).
 - b) Another episode of CL in Malaysia (row 42) which has no outcome yet, but is considered by the government since 2010 already (Government of India (2012)).
 - c) Two additional episodes in Brazil (rows 30 & 38) are added as these are not renewals but rather renegotiations due to a additional and subsequent CL threats (Wetzler and Ayala (2008)).
 - d) One additional CL was issued by Indonesia as World Health Organization (2008) and Intellectual Property Watch (2007) explain.
5. An Indian CL episode 2006-2007 on a cancer drug for export to Nepal was omitted since no government support from the Nepal side was reported.
6. In this list the World Bank income categorization is used rather than a mixture of World Bank and WTO classifications (World Bank Group (2012)). These are grouped according to 2011 gross national income per capita, for comparison converted by the "World Bank Atlas Method":
 - a) LIE: Low-income economies (\$1,025 or less),
 - b) LMIE: Lower-middle-income economies (\$1,026 to \$4,035) and
 - c) UMIE: Upper-middle-income economies (\$4,036 to \$12,475).

APPENDIX A. APPENDIX

Row	Episode Period	Nation	Population ^k in mio.	National Income Group ^l	Disease Group	Molecule	Outcome	IV	Royalty/ Discount	Type of Royalty	Sources
1	2001	Brazil	195	UMIE	HIV/AIDS	efavirenz	Discount	MERCK	60,0% -		a c
2	2001	Brazil	195	UMIE	HIV/AIDS	indinavir	Discount	MERCK	65,0% -		c
3	2001	Brazil	195	UMIE	HIV/AIDS	nefinavir	Discount	ROCHE	40,0% -		a c
4	2002	Zimbabwe	13	LIE	HIV/AIDS	all	CL	ALL			a
5	2002	Egypt	81	LMIE	NCD	sildenafil	CL	PFIZER			a
6	2003	Brazil	195	UMIE	HIV/AIDS	atanazavir	Discount	BMS	76,4% -		a c
7	2003	Malaysia	28	UMIE	HIV/AIDS	lamivudine	CL	GSK	waived by IV -		a j m
8	2003	Malaysia	28	UMIE	HIV/AIDS	didanosine	CL	BMS	waived by IV -		a j m
9	2003	Malaysia	28	UMIE	HIV/AIDS	zidovudine	CL	GSK	waived by IV -		a j m
10	2003	South Africa	50	UMIE	HIV/AIDS	lamivudine	VL	GSK	5,0% of net sales		a
11	2003	South Africa	50	UMIE	HIV/AIDS	nevirapine	VL	BI	5,0% of net sales		a
12	2003	South Africa	50	UMIE	HIV/AIDS	zidovudine	Discount	GSK	-		a
13	2003	South Africa	50	UMIE	HIV/AIDS	stavudine	Discount	BMS	-		a
14	2003	South Africa	50	UMIE	HIV/AIDS	didanosine	Discount	BMS	-		a
15	2003	South Africa	50	UMIE	HIV/AIDS	efavirenz	Discount	BMS	-		a
16	2003	South Africa	50	UMIE	HIV/AIDS	indinavir	Discount	MSD	-		a
17	2003	South Africa	50	UMIE	HIV/AIDS	abacavir	Discount	GSK	-		a
18	2004	Mozambique	23	LIE	HIV/AIDS	lamivudine	CL	GSK	20,0% of net sales		a
19	2004	Mozambique	23	LIE	HIV/AIDS	stavudine	CL	BMS	20,0% of net sales		a
20	2004	Mozambique	23	LIE	HIV/AIDS	nevirapine	CL	BI	20,0% of net sales		a
21	2004	Zambia	13	LMIE	HIV/AIDS	lamivudine	CL	GSK	2,5% of net sales		a i
22	2004	Zambia	13	LMIE	HIV/AIDS	stavudine	CL	BMS	2,5% of net sales		a i
23	2004	Zambia	13	LMIE	HIV/AIDS	nevirapine	CL	BI	2,5% of net sales		a i
24	2004	Indonesia	240	LMIE	HIV/AIDS	lamivudine	CL	GSK	0,5% of net sales		a g
25	2004	Indonesia	240	LMIE	HIV/AIDS	nevirapine	CL	BI	0,5% of net sales		a g
26	2005	Ghana	24	LMIE	HIV/AIDS	all	CL	ALL			a h
27	2006	Argentina	40	UMIE	CD	oseltamivir	VL	GILEAD			a
28	2006	Brazil	195	UMIE	HIV/AIDS	lopinavir	Discount	GILEAD	50,0% -		a
29	2006	Thailand	69	UMIE	HIV/AIDS	efavirenz	CL	MERCK	0,5%		a d
30	2007	Brazil	195	UMIE	HIV/AIDS	atanazavir	Discount	BMS	7,0% -		a c
31	2007	Thailand	69	UMIE	HIV/AIDS	lopinavir	CL	ABBOTT	0,5% of net sales		a d
32	2007	Thailand	69	UMIE	CVD	clopidogrel	CL	SANOFI-AVENTIS	0,5% of net sales		a d
33	2007	Thailand	69	UMIE	NCD	letrozole	CL	NOVARTIS	3%-5% of net sales		a d n
34	2007	Thailand	69	UMIE	NCD	docetaxel	CL	SANOFI-AVENTIS	3%-5% of net sales		a d n
35	2007	Thailand	69	UMIE	NCD	erlotinib	CL	ROCHE	3%-5% of net sales		a d n
36	2007	Indonesia	240	LMIE	HIV/AIDS	efavirenz	CL	MERCK	0,5%		f g
37	2007	Brazil	195	UMIE	HIV/AIDS	efavirenz	CL	MERCK	1,5%		a f
38	2007	Brazil	195	UMIE	HIV/AIDS	lopinavir	Discount	ABBOTT	3%-5% -		a c
39	2007	Rwanda/Canada	11	LIE	HIV/AIDS	lamivudine	CL	GSK	2,0%		a f
40	2007	Thailand	69	UMIE	NCD	Imatinib	Discount	NOVARTIS	100,0% -		a d
41	2010	Ecuador	14	UMIE	HIV/AIDS	ritonavir	CL	ABBOTT		Tiered Royalty Method	a b
42	2010	Malaysia	28	UMIE	HIV/AIDS	lopinavir	NA	ABBOTT	NA NA		o
43	2012	India	1.225	LMIE	NCD	sorafenib	CL	BAYER	6,0% of net sales		e

Figure A.1.: Complete list of compulsory licensing episodes (additional information)

The sources for the table are: a→ Beall and Kuhn (2012a)||b→ Saez (2010)||c→ Wetzler and Ayala (2008)||d→ Wetzler and Palmedo (2008)||e→ Government of India (2012)||f→ World Health Organization (2008)||g→ Intellectual Property Watch (2007)||h→ Government of Ghana (2005)||i→ Government of Zambia (2004)||j→ Government of Malaysia (2003)||k→ World Health Organization (2010b)||l→ World Bank Group (2012)||m→ Love (2004)||n→ Baker et al. (2008)||o→ Silverman (2012).

A.2. Excerpt: Agreement on Trade Related Aspects of Intellectual Property Rights

Article 31

Other Use Without Authorization of the Right Holder

Where the law of a Member allows for other use⁷ of the subject matter of a patent without the authorization of the right holder, including use by the government or third parties authorized by the government, the following provisions shall be respected:

- (a) authorization of such use shall be considered on its individual merits;
- (b) such use may only be permitted if, prior to such use, the proposed user has made efforts to obtain authorization from the right holder on reasonable commercial terms and conditions and that such efforts have not been successful within a reasonable period of time. This requirement may be waived by a Member in the case of a national emergency or other circumstances of extreme urgency or in cases of public non-commercial use. In situations of national emergency or other circumstances of extreme urgency, the right holder shall, nevertheless, be notified as soon as reasonably practicable. In the case of public non-commercial use, where the government or contractor, without making a patent search, knows or has demonstrable grounds to know that a valid patent is or will be used by or for the government, the right holder shall be informed promptly;
- (c) the scope and duration of such use shall be limited to the purpose for which it was authorized, and in the case of semi-conductor technology shall only be for public non-commercial use or to remedy a practice determined after judicial or administrative process to be anti-competitive;
- (d) such use shall be non-exclusive;
- (e) such use shall be non-assignable, except with that part of the enterprise or goodwill which enjoys such use;
- (f) any such use shall be authorized predominantly for the supply of the domestic market of the Member authorizing such use;
- (g) authorization for such use shall be liable, subject to adequate protection of the legitimate interests of the persons so authorized, to be terminated if and when the circumstances which led to it cease to exist and are unlikely to recur. The competent authority shall have the authority to review, upon motivated request, the continued existence of these circumstances;
- (h) the right holder shall be paid adequate remuneration in the circumstances of each case, taking into account the economic value of the authorization;
- (i) the legal validity of any decision relating to the authorization of such use shall be subject to judicial review or other independent review by a distinct higher authority in that Member;
- (j) any decision relating to the remuneration provided in respect of such use shall be subject to judicial review or other independent review by a distinct higher authority in that Member;

⁷"Other use" refers to use other than that allowed under Article 30.

APPENDIX A. APPENDIX

- (k) Members are not obliged to apply the conditions set forth in subparagraphs (b) and (f) where such use is permitted to remedy a practice determined after judicial or administrative process to be anti-competitive. The need to correct anti-competitive practices may be taken into account in determining the amount of remuneration in such cases. Competent authorities shall have the authority to refuse termination of authorization if and when the conditions which led to such authorization are likely to recur;
- (l) where such use is authorized to permit the exploitation of a patent ("the second patent") which cannot be exploited without infringing another patent ("the first patent"), the following additional conditions shall apply:
 - (i) the invention claimed in the second patent shall involve an important technical advance of considerable economic significance in relation to the invention claimed in the first patent;
 - (ii) the owner of the first patent shall be entitled to a cross-licence on reasonable terms to use the invention claimed in the second patent; and
 - (iii) the use authorized in respect of the first patent shall be non-assignable except with the assignment of the second patent.

Source: World Trade Organization (1994)

A.3. Implementation of Paragraph 6 of the Doha Declaration on the TRIPs Agreement and Public Health

Decision of 30 August 2003*

The General Council,

Having regard to paragraphs 1, 3 and 4 of Article IX of the Marrakesh Agreement Establishing the World Trade Organization ("the WTO Agreement");

Conducting the functions of the Ministerial Conference in the interval between meetings pursuant to paragraph 2 of Article IV of the WTO Agreement;

Noting the Declaration on the TRIPs Agreement and Public Health (WT/MIN(01)/DEC/2) (the "Declaration") and, in particular, the instruction of the Ministerial Conference to the Council for TRIPs contained in paragraph 6 of the Declaration to find an expeditious solution to the problem of the difficulties that WTO Members with insufficient or no manufacturing capacities in the pharmaceutical sector could face in making effective use of compulsory licensing under the TRIPs Agreement and to report to the General Council before the end of 2002;

Recognizing, where eligible importing Members seek to obtain supplies under the system set out in this Decision, the importance of a rapid response to those needs consistent with the provisions of this Decision;

Noting that, in the light of the foregoing, exceptional circumstances exist justifying waivers from the obligations set out in paragraphs (f) and (h) of Article 31 of the TRIPs Agreement with respect to pharmaceutical products;

Decides as follows:

1. For the purposes of this Decision:

- (a) "pharmaceutical product" means any patented product, or product manufactured through a patented process, of the pharmaceutical sector needed to address the public health problems as recognized in paragraph 1 of the Declaration. It is understood that active ingredients necessary for its manufacture and diagnostic kits needed for its use would be included¹;

* This Decision was adopted by the General Council in the light of a statement read out by the Chairman, which can be found in JOB(03)/177. This statement will be reproduced in the minutes of the General Council to be issued as WT/GC/M/82.

¹ This subparagraph is without prejudice to subparagraph 1(b).

APPENDIX A. APPENDIX

- (b) "eligible importing Member" means any least-developed country Member, and any other Member that has made a notification² to the Council for TRIPS of its intention to use the system as an importer, it being understood that a Member may notify at any time that it will use the system in whole or in a limited way, for example only in the case of a national emergency or other circumstances of extreme urgency or in cases of public non-commercial use. It is noted that some Members will not use the system set out in this Decision as importing Members³ and that some other Members have stated that, if they use the system, it would be in no more than situations of national emergency or other circumstances of extreme urgency;
- (c) "exporting Member" means a Member using the system set out in this Decision to produce pharmaceutical products for, and export them to, an eligible importing Member.

2. The obligations of an exporting Member under Article 31(f) of the TRIPS Agreement shall be waived with respect to the grant by it of a compulsory licence to the extent necessary for the purposes of production of a pharmaceutical product(s) and its export to an eligible importing Member(s) in accordance with the terms set out below in this paragraph:

- (a) the eligible importing Member(s)⁴ has made a notification² to the Council for TRIPS, that:
 - (i) specifies the names and expected quantities of the product(s) needed⁵;
 - (ii) confirms that the eligible importing Member in question, other than a least-developed country Member, has established that it has insufficient or no manufacturing capacities in the pharmaceutical sector for the product(s) in question in one of the ways set out in the Annex to this Decision; and
 - (iii) confirms that, where a pharmaceutical product is patented in its territory, it has granted or intends to grant a compulsory licence in accordance with Article 31 of the TRIPS Agreement and the provisions of this Decision⁶;
- (b) the compulsory licence issued by the exporting Member under this Decision shall contain the following conditions:
 - (i) only the amount necessary to meet the needs of the eligible importing Member(s) may be manufactured under the licence and the entirety of this production shall be exported to the Member(s) which has notified its needs to the Council for TRIPS;
 - (ii) products produced under the licence shall be clearly identified as being produced under the system set out in this Decision through specific labelling

² It is understood that this notification does not need to be approved by a WTO body in order to use the system set out in this Decision.

³ Australia, Austria, Belgium, Canada, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Japan, Luxembourg, the Netherlands, New Zealand, Norway, Portugal, Spain, Sweden, Switzerland, the United Kingdom and the United States.

⁴ Joint notifications providing the information required under this subparagraph may be made by the regional organizations referred to in paragraph 6 of this Decision on behalf of eligible importing Members using the system that are parties to them, with the agreement of those parties.

⁵ The notification will be made available publicly by the WTO Secretariat through a page on the WTO website dedicated to this Decision.

⁶ This subparagraph is without prejudice to Article 66.1 of the TRIPS Agreement.

APPENDIX A. APPENDIX

or marking. Suppliers should distinguish such products through special packaging and/or special colouring/shaping of the products themselves, provided that such distinction is feasible and does not have a significant impact on price; and

(iii) before shipment begins, the licensee shall post on a website⁷ the following information:

- the quantities being supplied to each destination as referred to in indent (i) above; and
- the distinguishing features of the product(s) referred to in indent (ii) above;

(c) the exporting Member shall notify⁸ the Council for TRIPS of the grant of the licence, including the conditions attached to it.⁹ The information provided shall include the name and address of the licensee, the product(s) for which the licence has been granted, the quantity(ies) for which it has been granted, the country(ies) to which the product(s) is (are) to be supplied and the duration of the licence. The notification shall also indicate the address of the website referred to in subparagraph (b)(iii) above.

3. Where a compulsory licence is granted by an exporting Member under the system set out in this Decision, adequate remuneration pursuant to Article 31(h) of the TRIPS Agreement shall be paid in that Member taking into account the economic value to the importing Member of the use that has been authorized in the exporting Member. Where a compulsory licence is granted for the same products in the eligible importing Member, the obligation of that Member under Article 31(h) shall be waived in respect of those products for which remuneration in accordance with the first sentence of this paragraph is paid in the exporting Member.

4. In order to ensure that the products imported under the system set out in this Decision are used for the public health purposes underlying their importation, eligible importing Members shall take reasonable measures within their means, proportionate to their administrative capacities and to the risk of trade diversion to prevent re-exportation of the products that have actually been imported into their territories under the system. In the event that an eligible importing Member that is a developing country Member or a least-developed country Member experiences difficulty in implementing this provision, developed country Members shall provide, on request and on mutually agreed terms and conditions, technical and financial cooperation in order to facilitate its implementation.

5. Members shall ensure the availability of effective legal means to prevent the importation into, and sale in, their territories of products produced under the system set out in this Decision and diverted to their markets inconsistently with its provisions, using the means already required to be available under the TRIPS Agreement. If any Member considers that such measures are proving insufficient for this purpose, the matter may be reviewed in the Council for TRIPS at the request of that Member.

⁷ The licensee may use for this purpose its own website or, with the assistance of the WTO Secretariat, the page on the WTO website dedicated to this Decision.

⁸ It is understood that this notification does not need to be approved by a WTO body in order to use the system set out in this Decision.

⁹ The notification will be made available publicly by the WTO Secretariat through a page on the WTO website dedicated to this Decision.

APPENDIX A. APPENDIX

6. With a view to harnessing economies of scale for the purposes of enhancing purchasing power for, and facilitating the local production of, pharmaceutical products:

- (i) where a developing or least-developed country WTO Member is a party to a regional trade agreement within the meaning of Article XXIV of the GATT 1994 and the Decision of 28 November 1979 on Differential and More Favourable Treatment Reciprocity and Fuller Participation of Developing Countries (L/4903), at least half of the current membership of which is made up of countries presently on the United Nations list of least-developed countries, the obligation of that Member under Article 31(f) of the TRIPS Agreement shall be waived to the extent necessary to enable a pharmaceutical product produced or imported under a compulsory licence in that Member to be exported to the markets of those other developing or least-developed country parties to the regional trade agreement that share the health problem in question. It is understood that this will not prejudice the territorial nature of the patent rights in question;
- (ii) it is recognized that the development of systems providing for the grant of regional patents to be applicable in the above Members should be promoted. To this end, developed country Members undertake to provide technical cooperation in accordance with Article 67 of the TRIPS Agreement, including in conjunction with other relevant intergovernmental organizations.

7. Members recognize the desirability of promoting the transfer of technology and capacity building in the pharmaceutical sector in order to overcome the problem identified in paragraph 6 of the Declaration. To this end, eligible importing Members and exporting Members are encouraged to use the system set out in this Decision in a way which would promote this objective. Members undertake to cooperate in paying special attention to the transfer of technology and capacity building in the pharmaceutical sector in the work to be undertaken pursuant to Article 66.2 of the TRIPS Agreement, paragraph 7 of the Declaration and any other relevant work of the Council for TRIPS.

8. The Council for TRIPS shall review annually the functioning of the system set out in this Decision with a view to ensuring its effective operation and shall annually report on its operation to the General Council. This review shall be deemed to fulfil the review requirements of Article IX:4 of the WTO Agreement.

9. This Decision is without prejudice to the rights, obligations and flexibilities that Members have under the provisions of the TRIPS Agreement other than paragraphs (f) and (h) of Article 31, including those reaffirmed by the Declaration, and to their interpretation. It is also without prejudice to the extent to which pharmaceutical products produced under a compulsory licence can be exported under the present provisions of Article 31(f) of the TRIPS Agreement.

10. Members shall not challenge any measures taken in conformity with the provisions of the waivers contained in this Decision under subparagraphs 1(b) and 1(c) of Article XXIII of GATT 1994.

11. This Decision, including the waivers granted in it, shall terminate for each Member on the date on which an amendment to the TRIPS Agreement replacing its provisions takes effect for that Member. The TRIPS Council shall initiate by the end of 2003 work on the preparation of such an amendment with a view to its adoption within six months, on the understanding that the amendment will be based, where appropriate, on this Decision and on the further understanding that it will not be part of the negotiations referred to in paragraph 45 of the Doha Ministerial Declaration (WT/MIN(01)/DEC/1).

Source: World Trade Organization (2003)